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Stereoselective synthesis of imidazolidin-2-ones via Pd-catalyzed alkene carboamination. Scope and limitations

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Abstract

A method for the synthesis of imidazolidin-2-ones from *N*-allylureas and aryl or alkenyl bromides via Pd-catalyzed carboamination reactions is described. The *N*-allylurea precursors are prepared in one step from readily available allylic amines and isocyanates, and the Pd-catalyzed reactions effect the formation of a C–C bond, a C–N bond, and up to two stereocenters in a single step. Good diastereoselectivities are obtained for the conversion of substrates bearing allylic substituents to 4,5-disubstituted imidazolidin-2-ones, and excellent selectivity for the generation of products resulting from *syn*-addition across the alkene is observed when substrates derived from cyclic alkenes or *E*-1,2-disubstituted alkenes are employed. A brief discussion of reaction mechanism and product stereochemistry is presented.

1. Introduction

Substituted imidazolidin-2-ones and other cyclic ureas are of considerable interest in pharmaceutical and medicinal chemistry, as many biologically active compounds contain these moieties. Cyclic ureas have been demonstrated to act as HIV protease inhibitors,¹ 5-HT₃ receptor antagonists,² and NK₁ antagonists.³ These structures have also been employed as monomeric units for biopolymer scaffolds that exhibit greater stability than typical peptides.⁴ In addition, imidazolidin-2-ones have found applications in organic synthesis as chiral auxiliaries,⁵ and as precursors to α -amino acids⁶ and vicinal diamines.⁷

Due to the utility of imidazolidin-2-ones, a number of methods have been developed for their construction. The most commonly employed method for the synthesis of these compounds involves generation of 1,2-diamines, which are then converted to cyclic ureas by treatment with phosgene, phosgene equivalents such as carbonyl diimidazole,⁸ or through other carbonylation methods.⁹ However, the preparation of 1,2-diamines frequently requires several steps, and is particularly cumbersome when the two amino groups bear different substituents.¹⁰

In order to overcome the limitations of classical methods for the preparation of imidazolidin-2-ones, several alternative strategies have been developed for the synthesis of these compounds.^{11,12,13,14,15,16} Despite these advances, few existing methods allow for ring-closure of a simple, readily available acyclic urea derivative, with formation of both a C–C and a C–N bond in the same step. Moreover, methods that accomplish this are limited in scope. For example,

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Pd-catalyzed Wacker-type carbonylation reactions of *N*-allylureas are limited to installation of ester functionality in the C–C bond-forming step.¹⁷ Two-step carboamination reactions of *N*-allylureas that involve ureidomercuration followed by radical coupling have been developed, but these methods require stoichiometric amounts of mercury reagents.¹⁸ Only one example of Pd-catalyzed carboamination of an *N*-propargylurea with acrolein has been reported, and this transformation does not lead to generation of new stereocenters.¹⁹

We recently reported a new strategy for the construction of imidazolidin-2-ones via Pd-catalyzed carboamination reactions^{20,21} between acyclic *N*-allylureas (**2**) and aryl bromides (eq 1).²² This method overcomes many limitations of existing approaches to the synthesis of these compounds. For example, the *N*-allylurea substrates (**2**) are prepared in one step and high yield from readily available allylic amines and isocyanates. The carboamination reactions generate two bonds (one C–C and one C–N) and up to two stereocenters in one step to afford products of general structure **3** with excellent diastereoselectivity. A number of different coupling partners can be employed, and preparation of derivatives bearing different substituents on N1 and N3 is straightforward. In this article we describe our full studies on the development, scope, and limitations of this transformation. These studies illustrate that both aryl and alkenyl halides can be employed as coupling partners in these reactions, and that the synthesis of imidazolidin-2-ones that are bicyclic or 4,5-disubstituted can be achieved with good to excellent levels of diastereoselectivity.

2. Results and Discussion

2.1. Optimization

In our preliminary studies we examined the Pd-catalyzed reaction of 1-allyl-3-ethyl-1-phenylurea (**4**) with 4-bromotoluene. Related experiments on the conversion of γ -aminoalkenes to pyrrolidines suggested that the choice of phosphine ligand would have a large impact on chemical yield.²⁰ Thus, a series of different phosphines were examined for the carboamination of **4**. As shown below (Table 1), treatment of **4** with 4-bromotoluene (1.2 equiv), NaOtBu (1.2 equiv), and catalytic amounts of Pd₂(dba)₃ (1 mol % complex, 2 mol % Pd) and phosphine ligand (2–4 mol %) in toluene (0.25 M) at 110 °C provided mixtures of the desired product **5** and oxidative cyclization product **6**. Use of dppb, dppe, or P(*o*-tol)₃ as ligand²³ afforded poor product ratios. However, when dppf, Dpe-phos, or Xantphos were employed as ligands,²³ the competing oxidative cyclization of **4** to **6** was suppressed. Under optimized conditions, the Pd₂(dba)₃/Xantphos-catalyzed coupling of **4** with 4-bromotoluene provided a 59% isolated yield of the imidazolidin-2-one **5**.

Initially, the modest yields obtained in the reactions described in Table 1 were puzzling, as ¹H NMR analysis of the crude reaction mixtures showed primarily the presence of **5** and **6**. To probe the possibility that volatile side products were generated, the Pd/Xantphos-catalyzed reaction of **4** with 4-bromotoluene was conducted in an NMR tube and monitored by ¹H NMR spectroscopy. This experiment indicated that significant amounts of *N*-allylaniline were generated in this transformation.²⁴ Control experiments demonstrated that the formation of *N*-allylaniline was base mediated, as the generation of *N*-allylaniline from **4** was also observed when **4** was heated with NaOtBu in the absence of Pd (eq 2).²⁵ Although additional optimization failed to improve reactions of **4**, cyclizations of related substrates bearing N3-aryl groups proceed in much higher yield (see below).

2.2. Synthesis of 4-Substituted Imidazolidin-2-ones

With optimized reaction conditions in hand, we proceeded to examine the scope of *N*-allylurea carboamination reactions that afford 4-substituted imidazolidin-2-one products (Table 2). A variety of aryl bromides are effective coupling partners in these transformations, including derivatives that are *o*-substituted (entries 4 and 13) or heteroaromatic (entry 9). In addition, a number of functional groups are tolerated, including nitriles (entry 7), *tert*-butyl esters (entry 12), trifluoromethyl groups (entry 10), and nonenolizable ketones (entry 11). Good yields are generally obtained with electron-neutral or electron-poor aryl bromides. However, use of electron-rich aryl bromides led to relatively low yields of the desired urea products. For example, the Pd-catalyzed reaction of **7** with 4-bromo-*t*-butylbenzene proceeded in 58% yield (entry 3), but the reaction of **7** with 4-bromoanisole afforded only 35% yield of **15** (entry 6).

In most cases, moderate yields of the desired imidazolidin-2-ones were obtained when substrates bearing *N*3-alkyl groups were employed due to competing base-mediated side reactions of these substrates. As noted in section 2.1, reactions of **4** generated significant amounts of *N*-allylaniline. Conversely, transformations of substrate **7** suffered from the formation of side products resulting from isomerization of the *N*-allyl group to a *N*-(1-propenyl) group.²⁶

In contrast to results obtained with *N*3-alkyl urea derivatives, good to excellent yields were obtained with urea substrates bearing *N*3-aryl groups. For example, although the reaction of 1-allyl-3-ethyl-1-methylurea (**7**) with 2-bromonaphthalene proceeded in only 68% yield (entry 5), the analogous coupling of 1-allyl-1-methyl-3-phenylurea (**9**) with 2-bromonaphthalene afforded a 97% yield of the imidazolidin-2-one **17** (entry 8). Of particular note, substrate **10** bearing an *N*1-benzyl group and an *N*3-PMP group (PMP = *p*-methoxyphenyl) was efficiently converted to the differentially protected imidazolidin-2-one products **21–23**. The *N*-benzyl and *N*-PMP-protecting groups can be removed independently to afford mono-protected products.²⁷ For example, treatment of **22** with ceric ammonium nitrate effected cleavage of the PMP group to afford **24** in 75% yield (eq 3). Alternatively, selective cleavage of the *N*-benzyl group was achieved through reduction with Li/NH₃ to provide **25** in 92% yield (eq 4).^{27a,28,29}

2.3. Synthesis of 4,4- and 4,5-Disubstituted Imidazolidin-2-ones

Having established the feasibility of generating 4-substituted imidazolidin-2-ones via Pd-catalyzed carboamination reactions of *N*-allylureas, we sought to extend the scope of this method to allow for the construction of more highly substituted products. As shown in Table

3, *N*-allylureas bearing allylic substituents were transformed to *trans*-4,5-disubstituted imidazolidin-2-ones upon treatment with an aryl bromide in the presence of NaOtBu and the Pd₂(dba)₃/Xantphos catalyst. The diastereoselectivity of these reactions was dependent on the size of the allylic substituent. For example, the Pd-catalyzed carboamination of methyl-substituted allylurea **26** provided **34** as an 8:1 mixture of diastereomers; **34** was obtained in 88% yield and 12:1 dr after chromatographic purification (Table 3, entry 1). Urea substrate **27** bearing a relatively large isopropyl group at the allylic position provided **35** in 83% yield with >20:1 dr (entry 2). Bicyclic 4,5-disubstituted imidazolidinones were also prepared in good yield with excellent diastereoselectivity through carboamination of 2-vinylpiperidine- or 2-vinylpyrrolidine-derived ureas **30** or **31** (entries 5–6).

Substrates that were *gem*-disubstituted or functionalized with a benzyloxymethyl group at the allylic position were transformed to the corresponding cyclic ureas in modest yields due to competing side reactions (entries 3–4). For example, the conversion of **28** to **36** proceeded in low yield due to both Pd-catalyzed oxidative cyclization and base-mediated isomerization of the starting alkene. The carboamination of **29** generated side products resulting from base-mediated hydroamination of the substrate.^{30,31} The hydroamination side reaction could be minimized by using Cs₂CO₃ in place of NaOtBu, but this modification resulted in the formation of other side products derived from oxidative cyclization and/or Heck arylation³² of the substrate.

The synthesis of 4,4-disubstituted imidazolidin-2-ones was accomplished via Pd-catalyzed carboamination reactions of *N*-allylurea derivatives **32** and **33** bearing 1,1-disubstituted alkenes. As shown in Table 3 (entries 7–9), these reactions proceed in good to excellent yield with several different aryl bromides.

2.4. Imidazolidin-2-ones Generated from Internal Olefins

The Pd-catalyzed carboamination of urea substrates bearing internal olefins leads to the formation of two new contiguous stereocenters with excellent stereocontrol. In all cases examined, these transformations occur with net *syn*-addition of the nitrogen atom and the aryl group across the C–C double bond. This stereochemical outcome is identical to that previously observed in related Pd-catalyzed carboamination reactions between γ -aminoalkenes and aryl bromides that afford pyrrolidine products.²⁰

As shown in Table 4, *E*-1,2-disubstituted alkene derivatives **43** and **44** were converted to **47**–**49** in moderate to good yield with >20:1 dr (entries 1–3). Interestingly, urea **43** was employed as a 4:1 mixture of *E/Z* alkene isomers, but imidazolidin-2-one **47** was obtained as a single stereoisomer (50% yield) that derives from *syn*-addition across the *E*-alkene; the unreacted *Z*-alkene substrate stereoisomer was observed in the crude reaction mixture.³³ Efforts to employ cinnamyl urea derivative **44** were initially hampered by the generation of significant amounts of side products resulting from base-mediated hydroamination.³¹ However, this side reaction could be minimized through use of Cs₂CO₃ in place of NaOtBu, and satisfactory yields of **48**–**49** were obtained after other minor adjustments to the reaction conditions.^{20g}

The Pd-catalyzed carboamination reactions were also effective with urea substrates derived from cycloalkenes (entries 4–5). For example, cyclopentene-derivative **45** was converted to **50** in 84% yield with >20:1 dr.³⁴ Efforts to couple the analogous cyclohexene derivative **46** with 4-bromotoluene were unsuccessful when a catalyst composed of Pd₂(dba)₃/Xantphos was employed. However, this carboamination reaction could be effected with excellent diastereoselectivity (albeit moderate yield) when PEt₃ was used in place of Xantphos as ligand. Interestingly, the product obtained under these conditions (**51**) was arylated at the 5-position rather than the expected 4-position.^{35,36}

2.5. Synthesis of 4-Allyl-imidazolidin-2-ones via Carboamination with Alkenyl Halides

In order to further expand the scope of the Pd-catalyzed carboamination reactions of *N*-allylurea derivatives, we briefly examined the use of alkenyl bromides as electrophilic coupling partners. As shown in Table 5, these transformations generally proceed in good yield to afford 4-allyl imidazolidin-2-one products. Interestingly, although the carboamination of **26** with an alkenyl halide proceeded with similar diastereoselectivity as observed with aryl bromide coupling partners, the reaction of **30** with *E*-bromopropene afforded a 1.5:1 mixture of diastereomers (entry 4). The origin of this diminished stereoselectivity relative to that obtained when **30** was coupled with bromobenzene (Table 3, entry 5) is not clear.

2.6. Proposed Mechanism and Origin of Side Products

On the basis of the observed product stereochemistry and the side products generated in these transformations, it is likely that the mechanism of Pd-catalyzed carboamination reactions of *N*-allylureas is analogous to that previously described for related transformations of γ -aminoalkenes that afford pyrrolidine products.²⁰ A plausible catalytic cycle that is consistent with the observations outlined above is illustrated in Scheme 1. Oxidative addition of the aryl/alkenyl halide to Pd(0) would generate **56**, which could be converted to Pd-amido complex **57** through reaction with the urea substrate/base combination. *Syn*-insertion of the alkene into the Pd–N bond would yield **58**, which could undergo C–C bond-forming reductive elimination to generate the observed imidazolidin-2-one product with concomitant regeneration of the Pd (0) catalyst.

Many of the side products observed in these reactions derive from competing β -hydride elimination of intermediate **58** in cases where C–C bond-forming reductive elimination may be relatively slow.³⁷ For example, β -hydride elimination of **58** would provide **59**, which could be converted to oxidative cyclization products **60** or **61** under the reaction conditions (Scheme 2).

The generation of unexpected isomer **51** in the Pd-catalyzed carboamination of **46** (Table 4, entry 5) also likely results from β -hydride elimination after *syn*-amidopalladation. As shown below (Scheme 3), β -hydride elimination from **63** would provide **64**. Reinsertion of the alkene into the Pd–H bond with the opposite regiochemistry would afford **65**, which could undergo reductive elimination to yield **51**. The conversion of **63** to **65** may be facilitated by the propensity of the small, electron-rich phosphine PEt_3 to slow the rate of C–C bond forming reductive elimination relative to β -hydride elimination.³⁷ It is likely that the conversion of **63** to **65** is also thermodynamically favorable, as the migration of the metal from C4 to C5 should alleviate a steric interaction between the metal and the N–Ph substituent.

2.7. Stereochemistry of Imidazolidin-2-one Products

On the basis of the mechanism shown in Scheme 1, it appears likely that the product stereochemistry is set in the alkene insertion step (**57**→**58**). The *syn*-alkene insertion results in net *syn*-addition of the nitrogen atom and the aryl group across the C–C double bond when cyclic or acyclic internal alkenes are employed as substrates (Table 4). The *syn*-addition selectivity is uniformly high (>20:1) in all examples examined thus far.

The *syn*-alkene insertion likely proceeds via an organized, cyclic transition state in which the allylic substituent is oriented to minimize unfavorable steric interactions, and the alkene π -bond is approximately eclipsed with the Pd–N bond.³⁸ As shown in Scheme 4, cyclization of low energy conformer **65** via transition state **66** would generate the observed *trans*-4,5-disubstituted imidazolidin-2-ones **34–36**. In contrast, conformer **68** should be higher in energy due to A(1,3)-strain, and transition state **69** suffers from unfavorable steric repulsion between

R⁴ and the Pd-bearing methylene group. As expected, selectivity is observed to improve with increasing size of R⁴ (Table 3).

The selectivity for the conversion of piperidine- and pyrrolidine-derived ureas **30** and **31** to bicyclic products **38** and **39** (Table 3, entries 5–6) appears to arise from cyclization through transition state **71** (Scheme 5), in which the 2-vinyl group is oriented in a pseudoequatorial position with its π -bond approximately eclipsed with the Pd–N bond. The observed major stereoisomer could also derive from cyclization via the more thermodynamically stable conformation, in which the alkenyl group is in a pseudoaxial position to minimize allylic strain interactions with the urea moiety. However, examination of molecular models indicates that the alkene and the metal are spatially distant in this conformation. The origin of differences in diastereoselectivity observed when aryl halides (>20:1 dr) vs. alkenyl halides (1.3:1 dr) are employed in the carboamination of **30** is unclear.

3. Summary and Conclusion

In conclusion, we have developed a concise synthesis of substituted imidazolidin-2-ones from readily available components (allylic amines, isocyanates, and aryl/alkenyl bromides). These transformations generate two bonds and up to two stereocenters in a single step, and afford the desired products in good yield with good to excellent levels of diastereoselectivity. Further studies are underway to apply these transformations to the synthesis of biologically active natural products and to develop catalytic asymmetric versions of these processes.

4. Experimental

4.1. General

All reagents were purchased from commercial sources and were used as obtained unless otherwise noted. Tris(dibenzylideneacetone)dipalladium (0) and all phosphine ligands were purchased from Strem Chemical Co. and used without further purification. All aryl bromides were obtained from commercial sources (Aldrich Chemical Co. or Acros Chemical Co.) and were used as obtained. *N*-Ethyl-2-methylallylamine was purchased from Aldrich Chemical Co. and used without purification. Toluene, THF, dichloromethane, and ether were purified using a Glass Contour solvent purification system. Product regiochemistry was assigned on the basis of ¹H NMR 2D-COSY and HSQC experiments. Product stereochemistry was assigned on the basis of ¹H NMR 2D-NOESY experiments. The stereochemistry of **47** was assigned on the basis of X-Ray crystallographic analysis, and the stereochemistry of **48–49** was assigned based on analogy to **47**. Yields refer to isolated yields of compounds estimated to be ≥95% pure as determined by ¹H NMR and either capillary GC or combustion analysis. All transformations described in this paper have been reproduced in duplicate or triplicate experiments, and averaged yields of these runs have been reported in the text and tables of this manuscript. However, since the yields reported in the Experimental Section describe the result of a single experiment, whereas the yields reported in Tables 2–5 are average yields of two or more experiments, the yields reported in the Experimental Section may differ from those shown in Tables 2–5. Reaction times described below have not been minimized.

4.2 General Procedure for the Synthesis of *N*-Allylurea Substrates

An oven- or flame-dried round bottom flask equipped with a stirbar was cooled under a stream of nitrogen and charged with the appropriate *N*-allylamine (1.0 equiv), the appropriate isocyanate (1.0–1.4 equiv), and isopropanol or CH₂Cl₂ (1.0 M). The reaction was stirred at room temperature until the starting amine had been completely consumed as judged by TLC or ¹H NMR analysis. The reaction mixture was then concentrated *in vacuo* and the crude product was purified via flash chromatography on silica gel.

4.2.1. 1-Allyl-3-ethyl-1-phenylurea (4)—Reaction of 1.57 g (11.8 mmol) of *N*-allylaniline with 1.17 g (16.5 mmol) of ethyl isocyanate following the general procedure afforded 2.22 g (92%) of the title compound as a yellow oil. ^1H NMR (500 MHz, CDCl_3) δ 7.38 (t, $J = 7.0$ Hz, 2 H), 7.28 (t, $J = 7.0$ Hz, 1 H), 7.22–7.18 (m, 2 H), 5.92–5.83 (m, 1 H), 5.08–5.01 (m, 2 H), 4.28–4.24 (m, 2 H), 4.19 (s, 1 H), 3.23–3.15 (m, 2 H), 1.00 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.0, 142.1, 134.9, 130.0, 128.7, 127.7, 117.0, 52.4, 35.7, 15.7; IR (film) 3354, 1653 cm^{-1} . Anal. calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.66; H, 8.02; N, 13.69.

4.2.2. 1-Allyl-3-ethyl-1-methylurea (7)—Reaction of 2.58 g (36.3 mmol) of *N*-methylallylamine with 3.60 g (50.6 mmol) of ethyl isocyanate following the general procedure afforded 4.79 g (94%) of the title compound as a clear oil. ^1H NMR (400 MHz, CDCl_3) δ 5.81–5.69 (m, 1 H), 5.18–5.14 (m, 1 H), 5.14–5.08 (m, 1 H), 4.33 (s, 1 H), 3.84 (d, $J = 5.6$ Hz, 2 H), 3.23 (q, $J = 7.2$ Hz, 2 H), 2.83 (s, 3 H), 1.09 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.1, 133.7, 116.1, 50.9, 35.5, 33.8, 15.5; IR (film) 3343, 1629 cm^{-1} . MS (ESI): 143.1178 (143.1184 calcd for $\text{C}_7\text{H}_{14}\text{N}_2\text{O}$, $\text{M} + \text{H}^+$).

4.2.3. 1-Allyl-3-benzyl-1-methylurea (8)—Reaction of 1.36 g (19.1 mmol) of *N*-methylallylamine with 2.54 g (19.1 mmol) of benzyl isocyanate following the general procedure afforded 3.26 g (83%) of the title compound as a white solid, m.p. 60–64 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.27–7.22 (m, 4 H), 7.20–7.17 (m, 1 H), 5.76–5.68 (m, 1 H), 5.12–5.10 (m, 1 H), 5.09–5.08 (m, 1 H), 4.97 (s, 1 H), 4.36 (d, $J = 5.5$ Hz, 2 H), 3.83–3.82 (m, 2 H), 2.81 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.2, 139.8, 133.8, 128.5, 127.5, 127.1, 116.4, 51.2, 44.9, 34.1; IR (film) 3336, 1634 cm^{-1} . Anal. calcd for $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.84; H, 7.96; N, 13.66.

4.2.4. 1-Allyl-1-methyl-3-phenylurea (9)—Reaction of 0.829 g (11.7 mmol) of *N*-methylallylamine with 1.94 g (16.3 mmol) of phenyl isocyanate following the general procedure afforded 1.82 g (82%) of the title compound as a white solid, m.p. 73–76 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.36–7.32 (m, 2 H), 7.29–7.23 (m, 2 H), 7.00 (t, $J = 7.2$ Hz, 1 H), 6.38 (s, br, 1 H), 5.91–5.81 (m, 1 H), 5.30–5.21 (m, 2 H), 3.98–3.94 (m, 2 H), 3.00 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.7, 139.3, 133.6, 129.1, 123.1, 119.9, 117.2, 51.8, 34.9; IR (film) 3288, 1636 cm^{-1} . Anal. calcd for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}$: C, 69.45; H, 7.42; N, 14.73. Found: C, 69.80; H, 7.59; N, 14.77.

4.2.5. 1-Allyl-1-benzyl-3-(4-methoxyphenyl)urea (10)—Reaction of 8.1 g (55.0 mmol) of *N*-allylbenzylamine with 8.2 g (55.0 mmol) of 4-methoxyphenylisocyanate following the general procedure afforded 12.82 g (79%) of the title compound as a white solid, m.p. 90–93 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.27 (m, 5 H), 7.19–7.16 (m, 2 H), 6.81–6.78 (m, 2 H), 6.26 (s, 1 H), 5.87–5.80 (m, 1 H), 5.30–5.24 (m, 2 H), 4.56 (s, 2 H), 3.95 (d, $J = 5.0$ Hz, 2 H), 3.75 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.3, 155.9, 137.8, 134.0, 132.3, 128.9, 127.7, 127.6, 122.2, 117.4, 114.1, 55.6, 50.6, 49.9; IR (film) 3322, 1634 cm^{-1} . Anal. calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.68; H, 6.80; N, 9.45.

4.2.6. 1-Benzyl-1-(but-3-en-2-yl)-3-(4-methoxyphenyl)urea (26)—Reaction of 1.33 g (8.25 mmol) of *N*-benzylbut-3-en-2-ylamine^{39,40} with 1.20 g (8.25 mmol) of 4-methoxyphenyl isocyanate according to the general procedure afforded 2.56 g (88%) of the title compound as a white solid, m.p. 95–97 °C. ^1H NMR (500 MHz, CDCl_3) δ 7.41–7.34 (m, 4 H), 7.34–7.29 (m, 1 H), 7.07 (d, $J = 9.0$ Hz, 2 H), 6.77 (d, $J = 9.0$ Hz, 2 H), 6.18 (s, 1 H), 5.99 (ddd, $J = 4.5, 11.0, 17.5$ Hz, 1 H), 5.29–5.22 (m, 2 H), 5.05–4.98 (m, 1 H), 4.54 (d, $J = 17.0$ Hz, 1 H), 4.37 (d, $J = 17.0$ Hz, 1 H), 3.75 (s, 3 H), 1.34 (d, $J = 7.0$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.1, 155.6, 139.3, 138.1, 132.1, 129.0, 127.7, 126.7, 121.8, 116.1,

113.9, 55.5, 52.3, 47.3, 16.5; IR (film) 3338, 1638 cm^{-1} . Anal calcd for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_2$: C, 73.52; H, 7.14; N, 9.03. Found: C, 73.75; H, 7.11; N, 9.13.

4.2.7. 1-Benzyl-3-(4-methoxyphenyl)-1-(4-methylpent-1-en-3-yl)urea (27)—A

flame dried round bottom flask equipped with a stirbar was cooled under a stream of nitrogen and charged with NaH (0.062 g, 1.55 mmol, 60% dispersion in mineral oil). The flask was purged with nitrogen and a solution of (*E*)-4-methylpent-2-en-1-ol⁴¹ (1.55 g, 15.5 mmol) in ether (2 mL) was added dropwise. The reaction mixture was cooled to -5°C and trichloroacetonitrile (2.24 g, 15.5 mmol) was added dropwise over 20 min. The reaction mixture was warmed to rt and stirred for 5 h, and then additional portions of NaH (0.062 g, 1.55 mmol, 60% dispersion in mineral oil), trichloroacetonitrile (0.5 mL, 5.0 mmol), and ether (5 mL) were added. The resulting mixture was stirred at rt for additional 6 h, and then concentrated *in vacuo*. The residue was diluted with pentane (15 mL) and methanol (0.04 mL). The resulting mixture was shaken vigorously for 1 min and then filtered through celite. The celite was rinsed with 15 mL of pentane and the solvent was removed *in vacuo*. The crude (*E*)-4-methylpent-2-enyl 2,2,2-trichloroacetimidate was transferred to a flame dried round bottom flask charged with a stirbar. Xylenes (100 mL) was added, and the resulting solution was heated to reflux with stirring for 8 h. The solution was then cooled to rt and filtered through a plug of silica gel. The plug was eluted with toluene and the resulting solution was concentrated *in vacuo*. The crude product was purified via flash chromatography to afford 3.05 g (80%) of 2,2,2-trichloro-*N*-(4-methylpent-1-en-3-yl)acetamide as an orange solid. ^1H NMR (400 MHz, CDCl_3) δ 6.57 (s, 1 H), 5.86–5.74 (m, 1 H), 5.25 (d, $J = 1.2$ Hz, 1 H), 5.22 (d, $J = 2.0$ Hz, 1 H), 4.34–4.27 (m, 1 H), 2.00–1.87 (m, 1 H), 0.99–0.95 (m, 6 H). A round bottom flask was purged with nitrogen and charged with 2,2,2-trichloro-*N*-(4-methylpent-1-en-3-yl)acetamide (2.97 g, 12.1 mmol), aqueous NaOH (60 mL, 6 M, 360 mmol), and 60 mL EtOH. The reaction mixture was heated to reflux for 1 h, then cooled to rt and stirred for 1.5 h. The mixture was then transferred to a separatory funnel and extracted with ether. The combined organic extracts were dried over anhydrous Na_2SO_4 and decanted into a round bottom flask. The flask was purged with nitrogen, cooled to 0°C , and triethylamine (6.7 mL, 48.4 mmol), benzoyl chloride (7.0 mL, 60.5 mmol), and 4-dimethylaminopyridine (0.15 g, 1.21 mmol) were added. The reaction mixture was stirred at rt for 27 h, then was quenched with aqueous NaHCO_3 and transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with EtOAc (3×150 mL). The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel to afford 2.16 g (88%) of *N*-(4-methylpent-1-en-3-yl)benzamide as a tan solid. ^1H NMR (500 MHz, CDCl_3) δ 7.81–7.77 (m, 2 H), 7.51 (t, $J = 7.0$ Hz, 1 H), 7.45 (t, $J = 7.5$ Hz, 2 H), 6.03 (d, $J = 7.5$ Hz, 1 H), 5.90–5.81 (m, 1 H), 5.26–5.17 (m, 2 H), 4.62–4.54 (m, 1 H), 2.00–1.89 (m, 1 H), 0.99 (d, $J = 3.5$ Hz, 3 H), 0.98 (d, $J = 3.5$ Hz, 3 H). A flame dried round bottom flask equipped with a stirbar was cooled under a stream of nitrogen and charged with *N*-(4-methylpent-1-en-3-yl)benzamide (1.68 g, 8.3 mmol) and cooled to 0°C . A solution of LiAlH_4 (34 mL, 34 mmol, 1.0 M in THF) was added and the solution was heated to reflux for 20 h. The reaction was placed in an ice bath and 1 mL water was slowly added followed by 1 mL 10M NaOH, 40 mL ether, and an additional 4 mL water. The solution was filtered through celite and the celite was rinsed with ether. The solvent was removed *in vacuo* to afford *N*-benzyl-4-methylpent-1-en-3-ylamine, which was then treated with 1.24 g (8.3 mmol) of 4-methoxyphenyl isocyanate for 2.5 h according to the general procedure to afford 2.36 g (84% over two steps) of the title compound as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 7.41–7.35 (m, 4 H), 7.35–7.29 (m, 1 H), 7.00 (d, $J = 9.0$ Hz, 2 H), 6.74 (d, $J = 9.0$ Hz, 2 H), 6.06 (s, 1 H), 5.86 (ddd, $J = 8.0, 10.5, 18.5$ Hz, 1 H), 5.31 (d, $J = 17.5$ Hz, 1 H), 5.24 (d, $J = 10.0$ Hz, 1 H), 4.56 (d, $J = 17.5$ Hz, 1 H), 4.44 (d, $J = 17.0$ Hz, 1 H), 4.48–4.39 (m, 1 H), 3.73 (s, 3 H), 2.09–1.98 (m, 1 H), 1.02 (d, $J = 7.0$ Hz, 3 H), 0.97 (d, $J = 6.5$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.0, 155.5, 137.5, 136.3, 132.0, 128.8, 127.6, 126.8, 121.8, 118.5, 113.8, 65.1,

55.3, 48.1, 29.9, 20.2, 19.5; IR (film) 3337, 1640 cm^{-1} . Anal calcd for $\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_2$: C, 74.52; H, 7.74; N, 8.28. Found: C, 74.28; H, 7.58; N, 8.16.

4.2.8. 1-Benzyl-1-(1-(benzyloxy)but-3-en-2-yl)-3-(4-methoxyphenyl)urea (28)—

(*Z*)-4-(benzyloxy)but-2-en-1-ol⁴² was converted to the title compound using a procedure analogous to that employed for the synthesis of **27**. This procedure afforded 1.59 g (20% overall yield) of the title compound as a clear oil. ^1H NMR (400 MHz, CDCl_3) δ 7.40–7.24 (m, 10 H), 7.20 (s, 1 H), 6.95 (d, J = 8.8 Hz, 2 H), 6.72 (d, J = 8.8 Hz, 2 H), 5.99–5.86 (m, 1 H), 5.32–5.20 (m, 2 H), 4.82–4.71 (m, 2 H), 4.54–4.40 (m, 3 H), 3.74 (s, 3 H), 3.77–3.71 (m, 1 H), 3.66 (dd, J = 7.2, 10.0 Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.8, 155.3, 138.8, 137.4, 134.4, 132.6, 128.7, 128.5, 128.1, 128.0, 127.4, 127.2, 121.2, 118.2, 113.9, 73.6, 71.3, 58.3, 55.5, 48.7; IR (film) 3334, 1657 cm^{-1} . Anal. calcd for $\text{C}_{26}\text{H}_{28}\text{N}_2\text{O}_3$: C, 74.97; H, 6.78; N, 6.73. Found: C, 75.00; H, 6.80; N, 6.75.

4.2.9. 1-Benzyl-3-(4-methoxyphenyl)-1-(2-methylbut-3-en-2-yl)urea (29)—A

flame-dried round bottom flask was cooled under a stream of nitrogen and charged with [Ir(COD)Cl]₂ (27 mg, 0.04 mmol), triphenyl phosphite (42 μL , 0.16 mmol), 2-methylbut-3-en-2-yl acetate⁴⁰ (256 mg, 2.0 mmol), benzylamine (643 mg, 6.0 mmol), and ethanol (4.4 mL). The resulting solution was heated to reflux under an atmosphere of nitrogen for 5 h. The solution was then cooled to rt, diluted with 25 mL of ether, transferred to a separatory funnel, and washed with 6M HCl (25 mL). The layers were separated, and the aqueous layer was taken to pH 10 through addition of 6M NaOH (10 mL). The aqueous layer was extracted with ether (2 $\times$ 25 mL), and the combined organic layers were dried over anhydrous Na_2SO_4 , filtered, and concentrated *in vacuo*. The crude product was purified via flash chromatography on silica gel to afford 177 mg (51%) of *N*-benzyl-2-methylbut-3-en-2-ylamine as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.37–7.27 (m, 4 H), 7.27–7.19 (m, 1 H), 5.84 (dd, J = 10.8, 17.2 Hz, 1 H), 5.14–5.06 (m, 2 H), 3.64 (s, 1 H), 1.24 (s, 6 H), 1.04 (s, 1 H). Reaction of *N*-benzyl-2-methylbut-3-en-2-ylamine (375 mg, 2.14 mmol) with 4-methoxyphenyl isocyanate (278 μL , 2.14 mmol) according to the general procedure afforded 574 mg (83%) of the title compound as a white solid, m.p. 81–85°C. ^1H NMR (500 MHz, CDCl_3) δ 7.39–7.34 (m, 4 H), 7.30–7.24 (m, 1 H), 7.16 (d, J = 9.0 Hz, 2 H), 6.79 (d, J = 9.0 Hz, 2 H), 6.76 (s, 1 H), 6.24 (dd, J = 10.5, 18.0 Hz, 1 H), 5.27 (d, J = 17.5 Hz, 1 H), 5.18 (d, J = 11.0 Hz, 1 H), 4.71 (s, 2 H), 3.75 (s, 3 H), 1.54 (s, 6 H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.0, 155.5, 147.1, 140.2, 132.3, 128.8, 127.0, 126.3, 121.5, 114.0, 112.3, 59.8, 55.5, 48.5, 26.5; IR (film) 3403, 1659 cm^{-1} . MS (ESI): 347.1741 (347.1735 calcd for $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.2.10. *N*-(4-Methoxyphenyl)-2-vinylpiperidine-1-carboxamide (30)—A

flame-dried round-bottom flask equipped with a stirbar was cooled under a stream of nitrogen and charged with *N*-(*tert*-butoxycarbonyl)-2-vinylpiperidine⁴³ (2.11 g, 10 mmol) and CH_2Cl_2 (100 mL). The solution was cooled to 0 °C and trifluoroacetic acid (15 mL, 202 mmol) was added. The reaction mixture was warmed to rt and stirred for 1 h, at which point the reaction was judged complete by TLC analysis. The reaction was quenched with 100 mL saturated aqueous NaHCO_3 and the resulting mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 $\times$ 150 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and decanted into a round-bottom flask equipped with a stirbar. The solution was cooled to 0 °C, 4-methoxyphenyl isocyanate (1.3 mL, 1.49 g, 10 mmol) was added, and the reaction was stirred at rt for 1.5 h. The reaction mixture was concentrated *in vacuo* and the crude product was purified by flash chromatography on silica gel to afford 2.04 g (78%) of the title compound as a white solid, m.p. 101–103 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.23 (d, J = 9.2 Hz, 2 H), 6.80 (d, J = 8.8 Hz, 2 H), 6.43 (s, br, 1 H), 5.82 (ddd, J = 4.0, 10.8, 17.6 Hz, 1 H), 5.26 (d, J = 10.4 Hz, 1 H), 5.16 (d, J = 17.2 Hz, 1 H), 4.71 (s, br, 1 H), 3.97 (d, J = 13.6 Hz, 1 H), 3.76 (s, 3 H), 2.97 (dt, J = 3.2, 12.0 Hz,

1 H), 1.84–1.71 (m, 2 H), 1.70–1.59 (m, 2 H), 1.57–1.42 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.9, 155.5, 136.5, 132.3, 122.1, 116.2, 113.9, 55.4, 53.1, 39.8, 29.2, 25.2, 19.2; IR (film) 3316, 1630 cm^{-1} . MS (ESI): 283.1418 (283.1422 calcd for $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.2.11. *N*-(4-Methoxyphenyl)-2-vinylpyrrolidine-1-carboxamide (31)—A flame-dried round-bottom flask equipped with a stirbar was cooled under a stream of nitrogen and charged with *N*-(tert-butoxycarbonyl)-2-vinylpyrrolidine⁴⁴ (0.647 g, 3.3 mmol) and CH_2Cl_2 (33 mL). The solution was cooled to 0 °C and trifluoroacetic acid (6 mL, 80.8 mmol) was added. The reaction mixture was warmed to rt and stirred for 4 h, at which point the reaction was judged complete by TLC analysis. The solvent was removed *in vacuo*, and the residue was redissolved in CH_2Cl_2 (20 mL). Solid K_2CO_3 (10 g) was added to the solution and the resulting suspension was stirred for 30 min then filtered through a fritted funnel. The solids were rinsed with CH_2Cl_2 (50 mL), and the resulting solution of 2-vinylpyrrolidine was transferred to a round-bottom flask and cooled to 0 °C. The solution was treated with 4-methoxyphenyl isocyanate (0.49 g, 0.33 mmol) according to the general procedure to afford 445 mg (55%) of the title compound as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.26 (d, J = 9.2 Hz, 2 H), 6.81 (d, J = 8.8 Hz, 2 H), 6.36 (s, 1 H), 5.90 (ddd, J = 6.8, 10.0, 16.8 Hz, 1 H), 5.34 (d, J = 16.8 Hz, 1 H), 5.27 (d, J = 10.4 Hz, 1 H), 4.32–4.23 (m, 1 H), 3.77 (s, 3 H), 3.69–3.58 (m, 1 H), 3.57–3.47 (m, 1 H), 2.24–2.12 (m, 1 H), 1.99–1.77 (m, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.1, 154.5, 139.2, 132.2, 121.2, 115.3, 113.6, 59.3, 55.2, 46.4, 32.6, 22.8; IR (film) 3318, 1648 cm^{-1} . MS (ESI): 247.1447 (247.1447 calcd for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2$, $\text{M} + \text{H}^+$).

4.2.12. 1-Ethyl-1-(2-methylallyl)-3-phenylurea (32)—Reaction of 0.99 g (10.0 mmol) of ethyl-(2-methylallyl)amine with 1.19 g (10.0 mmol) of phenyl isocyanate following the general procedure afforded 2.16 g (99%) of the title compound as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.33–7.30 (m, 2 H), 7.26–7.22 (m, 2 H), 7.00–6.96 (m, 1 H), 6.45 (s, 1 H), 5.012 (s, 1 H), 5.009 (s, 1 H), 3.82 (s, 2 H), 3.41 (q, J = 7.6 Hz, 2 H), 1.77 (s, 3 H), 1.18 (t, J = 6.8 Hz, 3 H); ^{13}C (125 MHz, CDCl_3) δ 155.6, 142.1, 139.4, 128.9, 122.9, 119.7, 112.3, 53.2, 42.8, 20.0, 13.6; IR (film) 3331, 1626 cm^{-1} . MS (EI): 218.1411 (218.1419 calcd for $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}$).

4.2.13. 1-Benzyl-3-(4-methoxyphenyl)-1-(2-methylallyl)urea (33)—Reaction of 1.61 g (10 mmol) of *N*-benzyl-2-methylprop-2-en-1-amine⁴⁵ with 1.49 g (10 mmol) of 4-methoxyphenyl isocyanate for 1 h according to the general procedure afforded 2.56 g (83%) of the title compound as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 7.39–7.27 (m, 5 H), 7.21 (d, J = 8.5 Hz, 2 H), 6.82 (d, J = 9.0 Hz, 2 H), 6.37 (s, 1 H), 5.02 (s, 1 H), 5.01 (s, 1 H), 4.59 (s, 2 H), 3.86 (s, 2 H), 3.77 (s, 3 H), 1.75 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.3, 155.7, 141.5, 137.7, 132.2, 128.7, 127.6, 127.5, 121.8, 114.0, 112.3, 55.5, 53.0, 50.6, 19.8; IR (film) 3332, 1640 cm^{-1} . MS (ESI): 333.1573 (333.1579 calcd for $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.2.14. (*E*)-1-(But-2-enyl)-1,3-diphenylurea (43)—Reaction of 0.973 g (6.61 mmol) of (*E*)-*N*-(but-2-enyl)aniline⁴⁶ (4:1 mixture of *E/Z* isomers) with 0.867 g, (7.27 mmol) of phenyl isocyanate according to the general procedure afforded 1.70 g (97%) of the title compound as a white solid, m.p. 61–65 °C. This material was obtained as a 4:1 mixture of *E/Z* isomers as judged by ^1H NMR analysis. Data are reported for the major isomer. ^1H NMR (400 MHz, CDCl_3) δ 7.45 (t, J = 7.2 Hz, 3 H), 7.36 (t, J = 7.2 Hz, 2 H), 7.32–7.17 (m, 4 H), 6.96 (t, J = 7.2 Hz, 1 H), 6.12 (s, 1 H), 5.63–5.48 (m, 2 H), 4.25 (d, J = 5.6 Hz, 2 H), 1.64 (d, J = 6.0 Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 154.1, 141.6, 139.0, 130.3, 129.0, 128.9, 128.8, 128.2, 126.9, 122.9, 119.3, 51.7, 17.9; IR (film) 3323, 1675 cm^{-1} . Anal. calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.58; H, 6.94; N, 10.52.

4.2.15. (*E*)-1-Benzyl-1-cinnamyl-3-(4-methoxyphenyl)urea (44)—Reaction of 1.21 g (5.4 mmol) of (*E*)-*N*-benzylcinnamylamine⁴⁷ with 0.81 g (5.4 mmol) of 4-methoxyphenyl isocyanate for 36 h according to the general procedure afforded 1.41 g (70%) of the title compound as a white solid, m.p. 127–130 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.44–7.23 (m, 10 H), 7.17 (d, *J* = 9.0 Hz, 2 H), 6.79 (d, *J* = 9.0 Hz, 2 H), 6.57 (d, *J* = 16.0 Hz, 1 H), 6.35 (s, 1 H), 6.21 (dt, *J* = 5.5, 15.5 Hz, 1 H), 4.62 (s, 2 H), 4.14 (d, *J* = 5.0 Hz, 2 H), 3.75 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 156.2, 155.8, 137.6, 136.1, 132.5, 132.0, 128.9, 128.7, 128.0, 127.7, 127.4, 126.4, 125.0, 122.0, 114.1, 55.5, 50.5, 49.5; IR (film) 3328, 1638 cm⁻¹. MS (ESI): 373.1927 (373.1916 calcd for C₂₄H₂₄N₂O₂, M + Na⁺).

4.2.16. 1-Benzyl-1-(cyclopent-2-enyl)-3-phenyl-urea (45)—*N*-Benzylcyclopent-2-enylamine was prepared from benzylamine (4.91 g, 45.8 mmol) and cyclopentadiene (6.04 g, 91.6 mmol) using Hartwig's procedure for hydroamination of cyclopentadiene.⁴⁸ This procedure generated 1.94 g (25%) of *N*-benzylcyclopent-2-enylamine as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.26 (m, 4 H), 7.24–7.20 (m, 1 H), 5.87–5.83 (m, 1 H), 5.82–5.80 (m, 1 H), 3.90–3.86 (m, 1 H), 3.83–3.77 (m, 2 H), 2.43–2.40 (m, 1 H), 2.28–2.16 (m, 2 H), 1.62–1.55 (m, 1 H), 1.28 (s, br, 1 H). Reaction of 1.94 g (11.2 mmol) of *N*-benzylcyclopent-2-enylamine with 1.33 g (11.2 mmol) of phenyl isocyanate following the general procedure afforded 3.0 g (92%) of the title compound as a white solid, m.p. 95–97 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.39–7.27 (m, 5 H), 7.20 (m, 4 H), 6.98–6.94 (m, 1 H), 6.48 (s, 1 H), 6.03–6.00 (m, 1 H), 5.75–5.73 (m, 1 H), 5.38–5.36 (m, 1 H), 4.46 (q, *J* = 10.8, 16.8 Hz, 2 H), 2.49–2.39 (m, 1 H), 2.37–2.29 (m, 2 H), 1.75–1.68 (m, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 155.9, 139.3, 138.4, 135.6, 131.6, 129.1, 128.9, 127.7, 126.9, 122.9, 119.7, 62.9, 48.1, 31.6, 28.6; IR (film) 3336, 1651 cm⁻¹. Anal. calcd for C₁₉H₂₀N₂O: C, 78.05; H, 6.89; N, 9.58. Found: C, 78.25; H, 6.93; N, 9.50.

4.2.17. 1-(Cyclohex-2-enyl)-1,3-diphenylurea (46)—*N*-(Cyclohex-2-enyl)aniline was prepared from aniline (1.17 mL, 12.82 mmol) and 1,3-cyclohexadiene (4.11 g, 51.3 mmol) using Hartwig's procedure for hydroamination of 1,3-cyclohexadiene.⁴⁹ This procedure generated 2.0 g (90%) of *N*-(cyclohex-2-enyl)aniline as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.15 (t, *J* = 7.2 Hz, 2 H), 6.67 (t, *J* = 4.4 Hz, 1 H), 6.61 (d, *J* = 8.0 Hz, 2 H), 5.86–5.81 (m, 1 H), 5.75–5.72 (m, 1 H), 3.98 (s, br, 1 H), 3.67 (s, br, 1 H), 2.10–1.94 (m, 2 H), 1.93–1.84 (m, 1 H), 1.76–1.54 (m, 3 H). Reaction of 1.96 g (11.0 mmol) of *N*-(cyclohex-2-enyl)aniline with 1.31 g (11.0 mmol) of phenyl isocyanate following the general procedure afforded 3.0 g (93%) of the title compound as a white solid, m.p. 122–125 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.47–7.38 (m, 3 H), 7.28–7.17 (m, 6 H), 6.95 (t, *J* = 7.0 Hz, 1 H), 5.93 (s, 1 H), 5.75–5.68 (m, 2 H), 5.35–5.28 (m, 1 H), 1.99–1.75 (m, 3 H), 1.68–1.52 (m, 2 H), 1.46–1.37 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 154.5, 139.2, 138.6, 131.0, 130.2, 130.0, 129.6, 128.9, 128.8, 122.9, 119.4, 52.5, 28.4, 24.6, 21.6; IR (film) 3326, 1672 cm⁻¹. Anal. calcd for C₁₉H₂₀N₂O: C, 78.05; H, 6.89; N, 9.58. Found: C, 77.73; H, 6.89; N, 9.46.

4.3. General Procedure for Pd-Catalyzed Synthesis of Imidazolidin-2-ones

An oven- or flame-dried Schlenk tube equipped with a stirbar was cooled under a stream of nitrogen and charged with Pd₂(dba)₃ (1 mol % complex, 2 mol % Pd), Xantphos (2 mol %), NaOtBu (1.2 equiv), the *N*-allylurea substrate (1.0 equiv), and the aryl bromide (1.2 equiv). The tube was purged with nitrogen, and undecane (0.125 equiv, internal standard) and toluene (4 mL/mmol urea substrate) were then added. If the acyclic urea and/or the aryl bromide were oils they were added at the same time as the toluene. The Schlenk tube was then heated to 110 °C with stirring until the starting material had been consumed as judged by GC or ¹H NMR analysis of aliquots removed from the reaction mixture. The mixture was then cooled to rt, saturated aqueous NH₄Cl (4–6 mL/mmol substrate) was added, and the mixture was extracted with methylene chloride or ethyl acetate (3 × 7 mL). The combined organic extracts were dried

over Na₂SO₄, filtered and concentrated *in vacuo*. The crude product was then purified by flash chromatography on silica gel.

4.3.1. 3-Ethyl-4-(4-methylbenzyl)-1-phenylimidazolidin-2-one (5)—Reaction of 102 mg (0.5 mmol) of 1-allyl-3-ethyl-1-phenylurea with 103 mg (0.6 mmol) of 4-bromotoluene for 1 h according to the general procedure afforded 91 mg (62%) of the title compound as a yellow solid, m.p. 93–95 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, *J* = 7.6 Hz, 2 H), 7.27 (t, *J* = 7.2 Hz, 2 H), 7.13 (d, *J* = 8.0 Hz, 2 H), 7.08 (d, *J* = 7.6 Hz, 2 H), 6.98 (t, *J* = 7.2 Hz, 1 H), 3.98–3.88 (m, 1 H), 3.73–3.60 (m, 2 H), 3.43 (dd, *J* = 6.4, 9.2 Hz, 1 H), 3.25–3.11 (m, 2 H), 2.59 (dd, *J* = 9.6, 13.6 Hz, 1 H), 2.33 (s, 3 H), 1.20 (t, *J* = 7.2 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 157.4, 140.7, 136.7, 133.4, 129.7, 129.1, 128.8, 122.2, 117.3, 53.0, 47.9, 38.7, 36.4, 21.2, 13.1; IR (film) 1704 cm^{−1}. Anal. calcd for C₁₉H₂₂N₂O: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.81; H, 7.68; N, 9.50.

4.3.1.1 3-Ethyl-4-methyl-1-phenyl-1,3-dihydroimidazol-2-one (6): This material was isolated as a side product in the Pd-catalyzed coupling of 1-allyl-3-ethyl-1-phenylurea with 4-bromotoluene as described in Table 1 and was characterized by ¹H NMR analysis. ¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, *J* = 8.0 Hz, 2 H), 7.39 (t, *J* = 7.2 Hz, 2 H), 7.19 (t, *J* = 7.2 Hz, 1 H), 6.31 (s, 1 H), 3.73 (q, *J* = 7.6 Hz, 14.8 Hz, 2 H), 2.12 (d, *J* = 1.6 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H).

4.3.2. 3-Ethyl-4-(naphthalen-2-ylmethyl)-1-phenylimidazolidin-2-one (11)—Reaction of 102 mg (0.5 mmol) of 1-allyl-3-ethyl-1-phenylurea with 124 mg (0.6 mmol) of 2-bromonaphthalene for 2 h according to the general procedure afforded 121 mg (73%) of the title compound as a lime green solid, m.p. 132–135 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.86–7.77 (m, 3 H), 7.66 (s, 1 H), 7.52–7.43 (m, 4 H), 7.32 (dd, *J* = 2.0, 10.5 Hz, 1 H), 7.30–7.23 (m, 2 H), 6.97 (t, *J* = 7.6 Hz, 1 H), 4.12–4.03 (m, 1 H), 3.76–3.61 (m, 2 H), 3.49 (dd, *J* = 6.0, 9.2 Hz, 1 H), 3.38 (dd, *J* = 4.0, 13.6 Hz, 1 H), 3.28–3.18 (m, 1 H), 2.78 (dd, *J* = 9.6, 13.2 Hz, 1 H), 1.23 (t, *J* = 6.8 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 157.4, 140.6, 134.1, 133.7, 132.6, 128.9, 128.8, 128.0, 127.9, 127.7, 127.3, 126.6, 126.1, 122.3, 117.4, 53.0, 48.0, 39.4, 36.5, 13.2; IR (film) 1703 cm^{−1}. Anal. calcd for C₂₂H₂₂N₂O: C, 79.97; H, 6.71; N, 8.48. Found: C, 80.00; H, 6.77; N, 8.32.

4.3.3. 4-(4-*tert*-Butylbenzyl)-3-ethyl-1-methylimidazolidin-2-one (12)—Reaction of 71 mg (0.5 mmol) of 1-allyl-3-ethyl-1-methylurea with 128 mg (0.6 mmol) of 1-bromo-4-*tert*-butylbenzene for 3 h according to the general procedure afforded 94 mg (69%) of the title compound as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.31 (d, *J* = 8.0 Hz, 2 H), 7.08 (d, *J* = 8.0 Hz, 2 H), 3.80–3.71 (m, 1 H), 3.60–3.49 (m, 1 H), 3.18–3.03 (m, 3 H), 2.91 (dd, *J* = 7.2, 8.8 Hz, 1 H), 2.70 (s, 3 H), 2.52 (dd, *J* = 10.0, 13.6 Hz, 1 H), 1.29 (s, 9 H), 1.11 (t, *J* = 7.2 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 161.3, 149.8, 133.9, 128.9, 125.7, 53.9, 51.0, 38.3, 36.5, 34.6, 31.5, 31.4, 13.0; IR (film) 1704 cm^{−1}. Anal. calcd for C₁₇H₂₆N₂O: C, 74.41; H, 9.55; N, 10.21. Found: C, 74.20; H, 9.61; N, 10.08.

4.3.4. 3-Ethyl-1-methyl-4-(naphthalen-1-ylmethyl)imidazolidin-2-one (13)—Reaction of 71 mg (0.5 mmol) of 1-allyl-3-ethyl-1-methylurea with 124 mg (0.6 mmol) of 1-bromonaphthalene for 4 h according to the general procedure afforded 91 mg (68%) of the title compound as a yellow oil. ¹H NMR (500 MHz, CDCl₃) δ 7.98 (d, *J* = 8.5 Hz, 1 H), 7.89–7.85 (m, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H), 7.57–7.48 (m, 2 H), 7.43–7.38 (m, 1 H), 7.32 (d, *J* = 6.5 Hz, 1 H), 4.02–3.94 (m, 1 H), 3.72–3.59 (m, 2 H), 3.24–3.16 (m, 1 H), 3.03–2.96 (m, 2 H), 2.92 (dd, *J* = 10.0, 14.0 Hz, 1 H), 2.72 (s, 3 H), 1.20 (t, *J* = 13.5 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 161.3, 134.1, 133.1, 132.0, 129.2, 127.8, 127.4, 126.5, 125.9, 125.6, 123.2, 52.9,

51.0, 36.7, 35.9, 31.4, 13.4; IR (film) 1699 cm^{-1} . Anal. calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}$: C, 76.09; H, 7.51; N, 10.44. Found: C, 75.97; H, 7.54; N, 10.37.

4.3.5. 3-Ethyl-1-methyl-4-(naphthalen-2-ylmethyl)imidazolidin-2-one (14)—

Reaction of 71 mg (0.5 mmol) of 1-allyl-3-ethyl-1-methylurea with 124 mg (0.6 mmol) of 2-bromonaphthalene for 4 h according to the general procedure afforded 91 mg (68%) of the title compound as a pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.84–7.75 (m, 3 H), 7.62 (s, 1 H), 7.51–7.41 (m, 2 H), 7.28 (dd, J = 1.6, 8.4 Hz, 1 H), 3.93–3.84 (m, 1 H), 3.64–3.53 (m, 1 H), 3.29 (dd, J = 4.4, 13.2 Hz, 1 H), 3.19–3.08 (m, 2 H), 2.96 (dd, J = 7.2, 8.8 Hz, 1 H), 2.72 (dd, J = 9.6, 13.2 Hz, 1 H), 2.71 (s, 3 H), 1.15 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.3, 134.5, 133.6, 132.4, 128.5, 127.8, 127.7, 127.6, 127.3, 126.4, 125.9, 53.8, 50.9, 39.1, 36.5, 31.3, 13.0; IR (film) 1699 cm^{-1} . MS (ESI): 291.1474 (291.1473 calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.3.6. 3-Ethyl-4-(4-methoxybenzyl)-1-methylimidazolidin-2-one (15)—

Reaction of 71 mg (0.5 mmol) of 1-allyl-3-ethyl-1-methylurea with 112 mg (0.6 mmol) of 4-bromoanisole for 4 h according to the general procedure afforded 48 mg (39%) of the title compound as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.07 (d, J = 8.4 Hz, 2 H), 6.83 (d, J = 8.8 Hz, 2 H), 3.87 (s, 3 H), 3.84–3.68 (m, 1 H), 3.60–3.43 (m, 1 H), 3.16–3.00 (m, 3 H), 2.89 (dd, J = 7.2, 8.8 Hz, 1 H), 2.70 (s, 3 H), 2.50 (dd, J = 9.6, 13.6 Hz, 1 H), 1.10 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.6, 155.9, 127.5, 126.2, 111.5, 52.7, 51.2, 48.1, 35.3, 33.8, 28.6, 10.3; IR (film) 1699 cm^{-1} . MS (ESI): 271.1408 (271.1422 calcd for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.3.7. 4-(3-Benzyl-1-methyl-2-oxo-imidazolidin-4-ylmethyl)benzonitrile (16)—

Reaction of 110 mg (0.54 mmol) of 1-allyl-3-benzyl-1-methylurea with 118 mg (0.65 mmol) of 4-bromobenzonitrile for 8 h according to the general procedure afforded 131 mg (80%) of the title compound as a white solid, m.p. 114–118 $^{\circ}\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.54 (d, J = 8.4 Hz, 2 H), 7.34–7.23 (m, 5 H), 7.12 (d, J = 8.0 Hz, 2 H), 4.83 (d, J = 15.2 Hz, 1 H), 4.07 (d, J = 15.2 Hz, 1 H), 3.61–3.54 (m, 1 H), 3.16–3.06 (m, 2 H), 2.90–2.86 (m, 1 H), 2.75 (s, 3 H), 2.65–2.60 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 161.2, 142.6, 137.2, 132.6, 130.1, 128.9, 128.3, 127.8, 118.8, 111.1, 53.4, 50.6, 46.4, 39.0, 31.4; IR (film) 2226, 1693 cm^{-1} . Anal. calcd for $\text{C}_{19}\text{H}_{19}\text{N}_3\text{O}$: C, 74.73; H, 6.27; N, 13.76. Found: C, 74.69; H, 6.26; N, 13.70.

4.3.8. 1-Methyl-4-(naphthalen-2-ylmethyl)-3-phenylimidazolidin-2-one (17)—

Reaction of 95 mg (0.5 mmol) of 1-allyl-1-methyl-3-phenylurea with 124 mg (0.6 mmol) of 2-bromonaphthalene for 1 h according to the general procedure afforded 153 mg (97%) of the title compound as an off-white solid, m.p. 122–126 $^{\circ}\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.83–7.76 (m, 3 H), 7.61–7.56 (m, 3 H), 7.51–7.37 (m, 4 H), 7.27 (dd, J = 1.6, 8.4 Hz, 1 H), 7.11 (t, J = 7.2 Hz, 1 H), 4.60–4.51 (m, 1 H), 3.37–3.26 (m, 2 H), 3.26–3.21 (m, 1 H), 2.83 (dd, J = 10.0, 14.0 Hz, 1 H), 2.79 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.5, 139.1, 134.3, 133.6, 132.5, 129.3, 128.6, 128.0, 127.9, 127.6, 127.4, 126.5, 126.0, 123.8, 121.1, 54.5, 49.4, 38.3, 31.3; IR (film) 1704 cm^{-1} . Anal. calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{O}$: C, 79.72; H, 6.37; N, 8.85. Found: C, 79.36; H, 6.38; N, 8.60.

4.3.9. 1-Methyl-3-phenyl-4-(pyridin-3-ylmethyl)imidazolidin-2-one (18)—

Reaction of 95 mg (0.5 mmol) of 1-allyl-1-methyl-3-phenylurea with 95 mg (0.6 mmol) of 3-bromopyridine for 30 min according to the general procedure afforded 120 mg (90%) of the title compound as a pale green solid, m.p. 150–151 $^{\circ}\text{C}$. ^1H NMR (500 MHz, CDCl_3) δ 8.48 (d, J = 4.0 Hz, 1 H), 8.41 (s, 1 H), 7.53–7.48 (m, 2 H), 7.43–7.40 (m, 1 H), 7.39–7.34 (m, 2 H), 7.24–7.19 (m, 1 H), 7.12–7.07 (m, 1 H), 4.53–4.46 (m, 1 H), 3.41 (t, J = 9.0 Hz, 1 H), 3.14 (dd, J = 5.0, 9.0 Hz, 1 H), 3.02 (dd, J = 3.0, 14.0 Hz, 1 H), 2.80 (dd, J = 8.5, 14.0 Hz, 1 H), 2.75 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.2, 150.4, 148.5, 138.7, 137.1, 132.2, 129.3,

124.0, 123.8, 121.0, 53.8, 49.1, 35.3, 31.1; IR (film) 1684 cm^{-1} . Anal. calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{O}$: C, 71.89; H, 6.41; N, 15.72. Found: C, 71.97; H, 6.37; N, 15.36.

4.3.10. 1-Methyl-3-phenyl-4-[4-(trifluoromethyl)benzyl]imidazolidin-2-one (19)—

Reaction of 95 mg (0.5 mmol) of 1-allyl-1-methyl-3-phenylurea with 135 mg (0.6 mmol) of 4-bromobenzotrifluoride for 1 h according to the general procedure afforded 158 mg (95%) of the title compound as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.52–7.49 (m, 4 H), 7.37 (t, J = 7.6 Hz, 2 H), 7.24 (t, J = 4.0 Hz, 2 H), 7.10 (t, J = 7.6 Hz, 1 H), 4.53–4.45 (m, 1 H), 3.38 (t, J = 8.8 Hz, 1 H), 3.18–3.09 (m, 2 H), 2.84–2.75 (m, 4 H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.0, 140.5, 138.6, 129.5, 129.1 (q, J = 32.3 Hz), 129.0, 125.5 (q, J = 3.7 Hz), 124.0 (q, J = 270.3), 123.6, 120.8, 53.8, 48.9, 37.7, 30.9; IR (film) 1706 cm^{-1} . Anal. calcd for $\text{C}_{18}\text{H}_{17}\text{F}_3\text{N}_2\text{O}$: C, 64.66; H, 5.13; N, 8.38. Found: C, 64.79; H, 5.13; N, 8.29.

4.3.11. 4-(4-Benzoylbenzyl)-1-methyl-3-phenylimidazolidin-2-one (20)—Reaction

of 95 mg (0.5 mmol) of 1-allyl-1-methyl-3-phenylurea with 157 mg (0.6 mmol) of 4-bromobenzophenone for 5 h according to the general procedure afforded 152 mg (82%) of the title compound as a white solid, m.p. 44–50 $^{\circ}\text{C}$. ^1H NMR (500 MHz, CDCl_3) δ 7.78–7.72 (m, 4 H), 7.58 (t, J = 7.5 Hz, 1 H), 7.55–7.50 (m, 2 H), 7.47 (t, J = 8.0 Hz, 2 H), 7.37 (t, J = 7.5 Hz, 2 H), 7.27–7.22 (m, 2 H), 7.10 (t, J = 7.0 Hz, 1 H), 4.56–4.49 (m, 1 H), 3.41 (t, J = 8.5 Hz, 1 H), 3.21–3.14 (m, 2 H), 2.82 (dd, J = 9.5, 14.0 Hz, 1 H), 2.80 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 196.3, 158.2, 141.5, 138.8, 137.6, 136.3, 132.6, 130.5, 130.0, 129.3, 129.1, 128.4, 123.7, 120.9, 54.0, 49.2, 38.1, 31.1; IR (film) 1704, 1656 cm^{-1} . Anal. calcd for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.58; H, 6.11; N, 7.43.

4.3.12. 4-[1-Benzyl-3-(4-methoxyphenyl)-2-oxoimidazolidin-1-ylmethyl]benzoic acid *tert*-butylester (21)—Reaction of 148 mg (0.5 mmol) of 1-allyl-1-benzyl-3-(4-

methoxyphenyl)urea with 154 mg (0.6 mmol) of 4-bromo-*tert*-butylbenzoate for 8 h according to the general procedure afforded 176 mg (75%) of the title compound as a yellow solid, m.p. 78–82 $^{\circ}\text{C}$. ^1H NMR (500 MHz, CDCl_3) δ 7.84 (d, J = 8.5 Hz, 2 H), 7.43 (d, J = 9.0 Hz, 2 H), 7.29–7.24 (m, 3 H), 7.12 (d, J = 6.5 Hz, 2 H), 7.04 (d, J = 8.0 Hz, 2 H), 6.94 (d, J = 8.5 Hz, 2 H), 4.39–4.28 (m, 3 H), 3.78 (s, 3 H), 3.21 (t, J = 9.0 Hz, 1 H), 3.01–2.97 (m, 2 H), 2.74 (dd, J = 5.0, 14.0 Hz, 1 H), 1.57 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.6, 158.3, 156.6, 141.2, 137.0, 131.7, 130.8, 129.8, 129.3, 128.7, 128.2, 127.6, 123.7, 114.6, 81.1, 55.6, 54.9, 48.1, 46.2, 38.1, 28.3; IR (film) 1700 cm^{-1} . Anal. calcd for $\text{C}_{29}\text{H}_{32}\text{N}_2\text{O}_4$: C, 73.70; H, 6.83; N, 5.93. Found: C, 73.40; H, 6.90; N, 5.81.

4.3.13. 1-Benzyl-3-(4-methoxyphenyl)-4-(2-methylbenzyl)imidazolidin-2-one (22)—Reaction of 148 mg (0.5 mmol) of 1-allyl-1-benzyl-3-(4-methoxyphenyl)urea with 103

mg (0.6 mmol) of 2-bromotoluene for 8 h according to the general procedure afforded 138 mg (71%) of the title compound as a white solid, m.p. 83–85 $^{\circ}\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.42–7.40 (m, 2 H), 7.33–7.19 (m, 5 H), 7.09–7.03 (m, 3 H), 6.93–6.91 (m, 3 H), 4.41 (s, 2 H), 4.32–4.29 (m, 1 H), 3.80 (s, 3 H), 3.20 (t, J = 8.8 Hz, 1 H), 3.08–3.00 (m, 2 H), 2.56 (dd, J = 3.6, 14.0 Hz, 1 H), 2.14 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.5, 156.6, 137.1, 136.4, 134.9, 131.7, 130.6, 129.7, 128.7, 128.3, 127.5, 126.9, 126.1, 124.1, 114.4, 55.5, 54.6, 48.1, 46.6, 35.5, 19.5; IR (film) 1699 cm^{-1} . Anal. calcd for $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}_2$: C, 77.69; H, 6.78; N, 7.25. Found: C, 77.80; H, 6.85; N, 7.33.

4.3.14. 1-Benzyl-4-(4-*tert*-butylbenzyl)-3-(4-methoxyphenyl)imidazolidin-2-one (23)—Reaction of 148 mg (0.5 mmol) of 1-allyl-1-benzyl-3-(4-methoxyphenyl)urea with 128

mg (0.6 mmol) of 1-bromo-4-*tert*-butylbenzene for 30 min according to the general procedure afforded 206 mg (97%) of the title compound as an orange oil. ^1H NMR (400 MHz, CDCl_3) δ 7.44 (d, J = 9.2 Hz, 2 H), 7.35–7.20 (m, 7 H), 6.99–6.92 (m, 4 H), 4.48–4.29 (m, 3 H), 3.82

(s, 3 H), 3.26 (t, $J = 8.8$ Hz, 1 H), 3.08 (dd, $J = 5.2, 8.8$ Hz, 1 H), 3.00 (dd, $J = 3.2, 13.6$ Hz, 1 H), 2.62 (dd, $J = 9.2, 13.6$ Hz, 1 H), 1.29 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.3, 156.1, 149.4, 136.9, 133.2, 131.6, 128.7, 128.4, 127.9, 127.2, 125.3, 123.3, 114.2, 55.3, 55.1, 47.8, 46.4, 37.5, 34.2, 31.2; IR (film) 1701 cm^{-1} . MS (ESI): 429.2523 (429.2542 calcd for $\text{C}_{28}\text{H}_{32}\text{N}_2\text{O}_2$, $\text{M} + \text{H}^+$).

4.3.15. ($\pm$)-(4*R*,5*R*)-4-[1-Benzyl-3-(4-methoxyphenyl)-5-methyl-2-oxoimidazolidin-4-ylmethyl]benzonitrile (34)—Reaction of 155 mg (0.5 mmol) of 1-benzyl-1-(but-3-en-2-yl)-3-(4-methoxyphenyl)urea with 109 mg (0.6 mmol) of 4-bromobenzonitrile for 1 h according to the general procedure afforded 181 mg (88%) of the title compound as a clear oil. This compound was isolated as a 12:1 mixture of diastereomers as judged by ^1H NMR analysis. The crude reaction mixture contained an 8:1 mixture of diastereomers. Data are for the major diastereomer. ^1H NMR (400 MHz, CDCl_3) δ 7.46 (d, $J = 8.0$ Hz, 2 H), 7.42 (d, $J = 8.8$ Hz, 2 H), 7.33–7.28 (m, 3 H), 7.24–7.10 (m, 2 H), 6.98 (d, $J = 8.4$ Hz, 2 H), 6.94 (d, $J = 9.2$ Hz, 2 H), 4.82 (d, $J = 15.2$ Hz, 1 H), 4.00–3.95 (m, 1 H), 3.95 (d, $J = 15.2$ Hz, 1 H), 3.83 (s, 3 H), 3.18 (dt, $J = 6.4, 11.2$ Hz, 1 H), 2.89 (dd, $J = 4.0, 14.0$ Hz, 1 H), 2.80 (dd, $J = 7.2$ Hz, 14.0 Hz, 1 H), 1.08 (d, $J = 6.4$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.0, 156.2, 141.6, 136.7, 132.0, 131.3, 130.1, 128.5, 127.9, 127.3, 123.2, 118.5, 114.3, 110.5, 61.8, 55.3, 51.0, 44.7, 37.2, 18.5; IR (film) $2227, 1697\text{ cm}^{-1}$. MS (ESI): 412.2013 (412.2025 calcd for $\text{C}_{26}\text{H}_{25}\text{N}_3\text{O}_2$, $\text{M} + \text{H}^+$).

4.3.16. ($\pm$)-(4*R*,5*R*)-1-Benzyl-5-isopropyl-3-(4-methoxyphenyl)-4-(4-methylbenzyl)imidazolidin-2-one (35)—Reaction of 169 mg (0.5 mmol) of 1-benzyl-3-(4-methoxyphenyl)-1-(4-methylpent-1-en-3-yl)urea with 103 mg (0.6 mmol) of 4-bromotoluene for 1 h according to the general procedure afforded 171 mg (85%) of the title compound as a yellow oil. This compound was isolated as a >20:1 mixture of diastereomers as judged by ^1H NMR analysis. The crude reaction mixture contained a >20:1 mixture of diastereomers. Data are for the major diastereomer. ^1H NMR (500 MHz, CDCl_3) δ 7.56 (d, $J = 9.0$ Hz, 2 H), 7.35–7.27 (m, 3 H), 7.17–7.12 (m, 2 H), 7.00 (d, $J = 8.0$ Hz, 2 H), 6.95 (d, $J = 9.0$ Hz, 2 H), 6.73 (d, $J = 8.0$ Hz, 2 H), 4.99 (d, $J = 15.5$ Hz, 1 H), 3.99 (dt, $J = 3.0, 8.5, 1\text{ H}$), 3.88 (d, $J = 15.5$ Hz, 1 H), 3.82 (s, 3 H), 3.09 (dd, $J = 2.5, 3.5$ Hz, 1 H), 2.80 (dd, $J = 3.0, 13.5$ Hz, 1 H), 2.51 (dd, $J = 8.5, 13.5$ Hz, 1 H), 2.29 (s, 3 H), 1.90–1.80 (m, 1 H), 0.76 (d, $J = 7.0$ Hz, 3 H), 0.46 (d, $J = 6.5$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.0, 155.6, 137.2, 136.0, 132.8, 131.9, 129.5, 129.0, 128.5, 128.0, 127.2, 122.0, 114.3, 58.6, 55.9, 55.4, 44.9, 37.9, 27.7, 21.0, 17.1, 15.0; IR (film) 1695 cm^{-1} . MS (ESI): 451.2374 (451.2361 calcd for $\text{C}_{28}\text{H}_{32}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.3.17 ($\pm$)-(4*R*,5*R*)-1-Benzyl-5-(benzyloxymethyl)-3-(4-methoxyphenyl)-4-(4-methylbenzyl)imidazolidin-2-one (36)—Reaction of 208 mg (0.5 mmol) of 1-benzyl-1-(1-(benzyloxy)but-3-en-2-yl)-3-(4-methoxyphenyl)urea with 103 mg (0.6 mmol) of 4-bromotoluene for 5 h according to the general procedure afforded 78 mg (31%) of the title compound as a yellow oil. This compound was isolated as a 20:1 mixture of diastereomers as judged by ^1H NMR analysis. The crude reaction mixture contained a 20:1 mixture of diastereomers. Data are for the major diastereomer. ^1H NMR (500 MHz, CDCl_3) δ 7.47 (d, $J = 9.0$ Hz, 2 H), 7.34–7.24 (m, 6 H), 7.17–7.09 (m, 4 H), 6.99 (d, $J = 8.0$ Hz, 2 H), 6.93 (d, $J = 9.0$ Hz, 2 H), 6.77 (d, $J = 7.5$ Hz, 2 H), 4.78 (d, $J = 15.0$ Hz, 1 H), 4.27 (s, 2 H), 4.17 (m, 1 H), 4.05 (d, $J = 15.5$ Hz, 1 H), 3.81 (s, 3 H), 3.37 (dd, $J = 5.0, 9.0$ Hz, 1 H), 3.27 (dd, $J = 5.0, 10.0$ Hz, 1 H), 3.21 (dd, $J = 5.0, 10.0$ Hz, 1 H), 2.89 (dd, $J = 3.0, 13.5$ Hz, 1 H), 2.57 (dd, $J = 8.5, 14.0$ Hz, 1 H), 2.29 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.4, 156.0, 137.7, 137.4, 136.1, 132.7, 131.9, 129.3, 129.2, 128.4, 128.3, 128.0, 127.6, 127.5, 127.2, 123.1, 114.3, 72.9, 69.8, 58.1, 55.4, 55.0, 45.8, 37.3, 21.0; IR (film) 1698 cm^{-1} . MS (ESI): 529.2458 (529.2467 calcd for $\text{C}_{33}\text{H}_{34}\text{N}_2\text{O}_3$, $\text{M} + \text{Na}^+$).

4.3.18 3-Benzyl-5-(biphenyl-4-ylmethyl)-1-(4-methoxyphenyl)-4,4-dimethylimidazolidin-2-one (37)—Reaction of 162 mg (0.5 mmol) of 1-benzyl-3-(4-methoxyphenyl)-1-(2-methylbut-3-en-2-yl)urea with 140 mg (0.6 mmol) of 4-bromobiphenyl for 4.5 h according to the general procedure afforded 79 mg (33%) of the title compound as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 6.8 Hz, 2 H), 7.46–7.37 (m, 4 H), 7.36–7.24 (m, 7 H), 7.24–7.17 (m, 1 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 4.50 (d, *J* = 15.6 Hz, 1 H), 4.28 (d, *J* = 15.6 Hz, 1 H), 4.13 (dd, *J* = 4.4, 9.2 Hz, 1 H), 3.75 (s, 3 H), 3.03 (dd, *J* = 4.4, 14.8 Hz, 1 H), 2.80 (dd, *J* = 9.2, 14.8 Hz, 1 H), 1.20 (s, 3 H), 0.99 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 158.6, 156.9, 140.6, 139.9, 139.1, 136.9, 131.8, 129.3, 128.7, 128.3, 127.6, 127.2, 127.0, 126.9, 126.8, 125.6, 114.1, 67.0, 59.8, 55.4, 43.1, 34.1, 26.7, 20.1; IR (film) 1698 cm⁻¹. MS (ESI): 477.2533 (477.2542 calcd for C₃₂H₃₂N₂O₂, M + H⁺).

4.3.19. (±)-(1*R*,8*aR*)-1-Benzyl-2-(4-methoxyphenyl)hexahydroimidazo[1,5-*a*]pyridin-3(5*H*)-one (38)—Reaction of 130 mg (0.5 mmol) of *N*-(4-methoxyphenyl)-2-vinylpiperidine-1-carboxamide with 94 mg (0.6 mmol) of bromobenzene for 1 h according to the general procedure afforded 137 mg (81%) of the title compound as a brown oil. This compound was isolated as a 20:1 mixture of diastereomers as judged by ¹H NMR analysis. The crude reaction mixture contained an 11:1 mixture of diastereomers. Data are for the major diastereomer. ¹H NMR (500 MHz, CDCl₃) δ 7.38 (d, *J* = 9.0 Hz, 2 H), 7.32–7.27 (m, 2 H), 7.25–7.21 (m, 1 H), 7.13 (d, *J* = 7.0 Hz, 2 H), 6.93 (d, *J* = 9.0 Hz, 2 H), 4.00–3.90 (m, 2 H), 3.81 (s, 3 H), 3.27–3.19 (m, 1 H), 3.07 (dd, *J* = 4.0, 14.0 Hz, 1 H), 2.74–2.61 (m, 2 H), 1.78–1.70 (m, 1 H), 1.62–1.54 (m, 1 H), 1.44–1.16 (m, 4 H); ¹³C NMR (100 MHz, CDCl₃) δ 156.8, 156.2, 136.6, 131.7, 129.1, 128.5, 126.6, 123.7, 114.2, 62.2, 57.1, 55.3, 40.8, 37.7, 30.9, 24.6, 23.2; IR (film) 1702 cm⁻¹. MS (ESI): 359.1738 (359.1735 calcd for C₂₁H₂₄N₂O₂, M + Na⁺).

4.3.20 (±)-(1*R*,7*aR*)-2-(4-Methoxyphenyl)-1-(3-(trifluoromethyl)benzyl)tetrahydro-1*H*-pyrrolo[1,2-*c*]imidazol-3(2*H*)-one (39)—Reaction of 62 mg (0.25 mmol) of *N*-(4-methoxyphenyl)-2-vinylpyrrolidine-1-carboxamide with 68 mg (0.3 mmol) of 3-bromobenzotrifluoride for 1 h according to the general procedure afforded 86 mg (88%) of the title compound as a yellow oil. This compound was isolated as a >20:1 mixture of diastereomers as judged by ¹H NMR analysis. The crude reaction mixture contained a 20:1 mixture of diastereomers. Data are for the major diastereomer. ¹H NMR (400 MHz, CDCl₃) δ 7.50 (d, *J* = 7.6 Hz, 1 H), 7.42 (t, *J* = 7.6 Hz, 1 H), 7.39–7.31 (m, 4 H), 6.92 (d, *J* = 9.2 Hz, 2 H), 4.29 (ddd, *J* = 2.4, 4.0, 9.6 Hz, 1 H), 3.81 (s, 3 H), 3.76–3.66 (m, 1 H), 3.50–3.41 (m, 1 H), 3.14 (dd, *J* = 3.6, 13.6 Hz, 1 H), 3.14–3.03 (m, 1 H), 2.85 (dd, *J* = 9.2, 14.0 Hz, 1 H), 2.02–1.88 (m, 1 H), 1.88–1.68 (m, 2 H), 1.46–1.29 (m, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 161.1, 156.3, 137.7, 132.6, 131.0, 130.8 (q, *J* = 32.2 Hz), 129.0, 125.8 (q, *J* = 3.6 Hz), 123.9 (q, *J* = 270.3 Hz), 123.6 (q, *J* = 3.7 Hz), 123.4, 114.4, 60.8, 60.8, 55.4, 45.1, 38.4, 30.8, 24.6; IR (film) 1702 cm⁻¹. MS (ESI): 391.1634 (391.1633 calcd for C₂₁H₂₁F₃N₂O₂, M + H⁺).

4.3.21. 1-Ethyl-4-methyl-3-phenyl-4-(3-trifluoromethylbenzyl)imidazolidin-2-one (40)—Reaction of 109 mg (0.5 mmol) of 1-ethyl-1-(2-methylallyl)-3-phenylurea with 135 mg (0.6 mmol) of 3-bromobenzotrifluoride according to a slight modification of the general procedure in which the urea was added to the reaction mixture as a 0.25 M solution in toluene afforded 154 mg (81%) of the title compound as a yellow oil. ¹H NMR (500 MHz, CDCl₃) δ 7.50 (d, *J* = 8.0 Hz, 1 H), 7.42–7.38 (m, 3 H), 7.35–7.27 (m, 5 H), 3.41 (d, *J* = 9.0 Hz, 1 H), 3.37–3.31 (m, 1 H), 3.23–3.15 (m, 1 H), 3.09 (d, *J* = 16.0 Hz, 1 H), 2.92 (d, *J* = 9.0 Hz, 1 H), 2.76 (d, *J* = 13.5 Hz, 1 H), 1.29 (s, 3 H), 1.07 (t, *J* = 7.0 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 159.1, 137.6, 136.9, 133.7, 130.8 (q, *J* = 32.2 Hz), 129.4, 129.2, 129.0, 127.2, 127.0 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 271 Hz), 123.9 (q, *J* = 3.7 Hz), 60.5, 53.0, 44.4, 38.4, 24.7, 12.8; IR (film) 1701 cm⁻¹. MS (ESI): 385.1501 (385.1504 calcd for C₂₀H₂₁F₃N₂O M + Na⁺).

4.3.22. 1-Ethyl-4-methyl-4-(2-methylbenzyl)-3-phenylimidazolidin-2-one (41)—

Reaction of 109 mg (0.5 mmol) of 1-ethyl-1-(2-methylallyl)-3-phenylurea with 103 mg (0.6 mmol) of 2-bromotoluene for 5 h according to the general procedure afforded 135 mg (88%) of the title compound as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 7.41 (t, $J = 8.0$ Hz, 2 H), 7.34–7.28 (m, 3 H), 7.19–7.08 (m, 4 H), 3.44–3.34 (m, 2 H), 3.32–3.22 (m, 1 H), 3.05 (d, $J = 13.5$ Hz, 1 H), 2.92 (d, $J = 8.5$ Hz, 1 H), 2.79 (d, $J = 14.0$ Hz, 1 H), 2.25 (s, 3 H), 1.33 (s, 3 H), 1.13 (t, $J = 7.5$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.2, 137.0, 136.8, 134.8, 130.6, 130.6, 129.3, 128.8, 126.8, 126.7, 125.7, 61.4, 53.1, 39.8, 38.5, 24.7, 20.0, 12.6; IR (film) 1698 cm^{-1} . Anal calcd for $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.54; H, 7.91; N, 9.01.

4.3.23. 1-Benzyl-3-(4-methoxyphenyl)-4-methyl-4-(4-methylbenzyl)imidazolidin-2-one (42)—

Reaction of 155 mg (0.5 mmol) of 1-benzyl-3-(4-methoxyphenyl)-1-(2-methylallyl)urea with 103 mg (0.6 mmol) of 4-bromotoluene for 7.5 h according to the general procedure afforded 195 mg (97%) of the title compound as a yellow oil. ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.33 (m, 2 H), 7.32–7.28 (m, 3 H), 7.23 (d, $J = 9.0$ Hz, 2 H), 6.99 (d, $J = 7.5$ Hz, 2 H), 6.95 (d, $J = 9.0$ Hz, 2 H), 6.81 (d, $J = 8.0$ Hz, 2 H), 4.54 (d, $J = 15.0$ Hz, 1 H), 4.34 (d, $J = 15.0$ Hz, 1 H), 3.84 (s, 3 H), 3.32 (d, $J = 9.5$ Hz, 1 H), 2.88 (d, $J = 13.0$ Hz, 1 H), 2.75 (d, $J = 9.0$ Hz, 1 H), 2.64 (d, $J = 13.0$ Hz, 1 H), 2.28 (s, 3 H), 1.19 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.4, 158.5, 137.3, 136.1, 133.1, 131.0, 130.0, 129.1, 128.8, 128.4, 128.2, 127.3, 114.1, 60.6, 55.3, 52.7, 47.9, 43.7, 24.0, 20.8; IR (film) 1699 cm^{-1} . MS (ESI): 423.2042 (423.2048 calcd for $\text{C}_{26}\text{H}_{28}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.3.24. (±)-(1'S,4R)-4-1'-[(4-Benzhydrylideneamino)phenyl]ethyl-1,3-diphenylimidazolidin-2-one (47)—

Reaction of 133 mg (0.50 mmol) of (*E*)-1-(but-2-enyl)-1,3-diphenyl urea (4:1 mixture of *E*:*Z* isomers) with 202 mg (0.6 mmol) of benzhydrylidene-(4-bromophenyl)amine⁵⁰ for 8 h according to the general procedure afforded 132 mg (51%) of the title compound as a yellow solid, m.p. 190–194 °C. Analysis of the crude reaction mixture by ^1H NMR indicated that the desired product had formed with >20:1 dr. ^1H NMR (400 MHz, CDCl_3) δ 7.74–7.72 (m, 2 H), 7.57–7.52 (m, 4 H), 7.48–7.38 (m, 5 H), 7.35–7.31 (m, 2 H), 7.29–7.22 (m, 3 H), 7.19–7.02 (m, 6 H), 6.71 (d, $J = 8.4$ Hz, 2 H), 4.63–4.59 (m, 1 H), 3.52–3.45 (m, 2 H), 3.36–3.33 (m, 1 H), 1.11 (d, $J = 7.2$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.9, 155.5, 150.4, 140.2, 139.7, 138.0, 136.5, 135.7, 131.1, 129.8, 129.5, 129.3, 129.0, 128.8, 128.5, 128.1, 127.7, 124.7, 123.0, 122.5, 121.6, 118.0, 57.3, 42.8, 37.3, 10.5; IR (film) 1707, 1597 cm^{-1} . MS (ESI): 522.2546 (522.2545 calcd for $\text{C}_{36}\text{H}_{31}\text{N}_3\text{O}$, $\text{M} + \text{H}^+$).

4.3.25. (±)-(1'S,4R)-4-[[1-Benzyl-3-(4-methoxyphenyl)-2-oxoimidazolidin-4-yl](phenyl)methyl]benzonitrile (48)—

Reaction of 186 mg (0.5 mmol) of 1-benzyl-1-cinnamyl-3-(4-methoxyphenyl)urea with 109 mg (0.6 mmol) of 4-bromobenzonitrile for 26 h according to a modified general procedure where $\text{Pd}(\text{OAc})_2$ was used as the Pd source, Cs_2CO_3 was used as the base, dioxane was used as solvent and a reaction temperature of 100 °C afforded 179 mg (76%) of the title compound as a yellow oil. Analysis of the crude reaction mixture by ^1H NMR indicated that the desired product had formed with >20:1 dr. ^1H NMR (400 MHz, CDCl_3) δ 7.44 (d, $J = 8.4$ Hz, 2 H), 7.30–7.22 (m, 6 H), 7.19 (d, $J = 8.8$ Hz, 2 H), 7.15 (d, $J = 8.0$ Hz, 2 H), 7.07–7.01 (m, 2 H), 7.00–6.94 (m, 2 H), 6.78 (d, $J = 9.2$ Hz, 2 H), 4.99 (p, $J = 5.2$ Hz, 1 H), 4.40 (d, $J = 6.0$ Hz, 1 H), 4.26 (s, 2 H), 3.78 (s, 3 H), 3.52 (t, $J = 9.2$ Hz, 1 H), 3.20 (dd, $J = 4.4, 9.2$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.9, 156.3, 146.3, 138.3, 136.4, 132.0, 131.4, 129.1, 128.6, 128.4, 127.7, 127.3, 127.2, 124.3, 118.4, 114.0, 110.3, 56.2, 55.3, 52.9, 47.6, 45.2 (one carbon signal is absent due to incidental equivalence); IR (film) 2227, 1698 cm^{-1} . MS (ESI): 474.2181 (474.2182 calcd for $\text{C}_{31}\text{H}_{27}\text{N}_3\text{O}_2$, $\text{M} + \text{Na}^+$).

4.3.26 (±)-(1'S,4R)--1-Benzyl-4-[6-methoxynaphthalen-2-yl(phenyl)methyl]-3-(4-methoxyphenyl)imidazolidin-2-one (49)—Reaction of 93 mg (0.25 mmol) of 1-benzyl-1-cinnamyl-3-(4-methoxyphenyl)urea with 71 mg (0.3 mmol) of 2-bromo-6-methoxynaphthalene for 14 h according to a modified general procedure where Pd(OAc)₂ was used as the Pd source, Cs₂CO₃ was the base, dioxane was the solvent, and 100 °C was the reaction temperature afforded 97 mg (73%) of the title compound as an off-white solid, m.p. 86–92 °C. Analysis of the crude reaction mixture by ¹H NMR indicated that the desired product had formed with >20:1 dr. ¹H NMR (400 MHz, CDCl₃) δ 7.60 (dd, *J* = 8.8, 16.4 Hz, 2 H), 7.40 (d, *J* = 8.8 Hz, 3 H), 7.26–7.17 (m, 6 H), 7.13 (dd, *J* = 2.4, 8.8 Hz, 1 H), 7.09–7.04 (m, 2 H), 7.01–6.95 (m, 2 H), 6.94–6.89 (m, 2 H), 6.83 (d, *J* = 9.2 Hz, 2 H), 5.14 (dt, *J* = 4.0, 9.6 Hz, 1 H), 4.62 (d, *J* = 3.6 Hz, 1 H), 4.20 (q, *J* = 15.2 Hz, 2 H), 3.88 (s, 3 H), 3.73 (s, 3 H), 3.63 (t, *J* = 9.2 Hz, 1 H), 3.38 (dd, *J* = 4.4, 8.8 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 157.8, 157.6, 155.8, 139.2, 136.6, 135.8, 133.2, 131.7, 129.4, 129.1, 128.5, 128.4, 128.3, 127.8, 127.7, 127.2, 127.1, 126.9, 126.1, 123.1, 119.0, 114.2, 105.5, 55.8, 55.4, 55.3, 50.5, 47.7, 44.6; IR (film) 1698 cm⁻¹. MS (ESI): 529.2497 (529.2491 calcd for C₃₅H₃₂N₂O₃, M + H⁺).

4.3.27. (±)-(3a*S*,4*R*,6a*R*)-1-Benzyl-3-phenyl-4-(*p*-tolyl)hexahydrocyclopentaimidazol-2-one (50)—Reaction of 150 mg (0.51 mmol) of 1-benzyl-1-cyclopent-2-enyl-3-phenylurea with 105 mg (0.62 mmol) of 4-bromotoluene for 8 h according to the general procedure afforded 172 mg (88%) of the title compound as a white solid, m.p. 170–174 °C. Analysis of the crude reaction mixture by ¹H NMR indicated that the desired product had formed with >20:1 dr. ¹H NMR (500 MHz, CDCl₃) δ 7.34–7.31 (m, 4 H), 7.30–7.24 (m, 1 H), 7.06 (d, *J* = 8.5 Hz, 1 H), 6.94–6.91 (m, 5 H), 6.75–6.70 (m, 3 H), 4.90 (d, *J* = 15.5 Hz, 1 H), 4.78 (t, *J* = 7.5 Hz, 1 H), 4.15 (d, *J* = 15.0 Hz, 1 H), 4.10–4.07 (m, 1 H), 3.21–3.16 (m, 1 H), 2.15–2.06 (m, 5 H), 1.94–1.89 (m, 1 H), 1.67–1.59 (m, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 158.7, 140.0, 137.3, 136.2, 135.2, 129.2, 128.8, 128.63, 128.60, 127.9, 127.7, 122.1, 120.2, 61.1, 58.5, 51.4, 45.9, 29.9, 29.3, 21.0; IR (film) 1699 cm⁻¹. MS (ESI): 405.1957 (405.1943 calculated for C₂₆H₂₆N₂O, M + Na⁺).

4.3.28. (±)-(3a*S*,5*R*,7a*R*)-1,3-Diphenyl-5-(*p*-tolyl)octahydrobenzimidazol-2-one (51)—Reaction of 50 mg (0.17 mmol) of 1-(cyclohex-2-enyl)-1,3-diphenylurea with 35 mg (0.21 mmol) of 4-bromotoluene for 8 h according to the general procedure using PEt₃•HBF₄ (4 mol %) in place of Xantphos afforded 33 mg (50%) of the title compound as a grey solid, m.p. 195–198 °C. Analysis of the crude reaction mixture by ¹H NMR indicated that the desired product had formed with >20:1 dr. ¹H NMR (400 MHz, CDCl₃) δ 7.64–7.62 (m, 2 H), 7.44–7.40 (m, 2 H), 7.33–7.21 (m, 5 H), 7.08–7.00 (m, 5 H), 4.46–4.40 (m, 1 H), 4.32–4.29 (m, 1 H), 2.55–2.49 (m, 1 H), 2.36–2.29 (m, 1 H), 2.28–2.23 (m, 1 H), 2.26 (s, 3 H), 1.82–1.59 (m, 4 H); ¹³C (125 MHz, CDCl₃) δ 157.3, 142.6, 139.1, 138.1, 136.2, 129.4, 129.2, 126.7, 126.0, 125.3, 123.4, 119.9, 55.4, 53.6, 40.0, 35.6, 28.0, 25.4, 21.2 (one carbon signal is absent due to incidental equivalence); IR (film) 1702 cm⁻¹. MS (ESI): 405.1960 (405.1943 calcd for C₂₆H₂₆N₂O, M + Na⁺).

4.3.29. (*E*)-1-Benzyl-4-cinnamyl-3-(4-methoxyphenyl)imidazolidin-2-one (52)—Reaction of 148 mg (0.5 mmol) of 1-allyl-1-benzyl-3-(4-methoxyphenyl)urea with 183 mg (1.0 mmol) of β-bromostyrene for 3 h according to the general procedure afforded 147 mg (74%) of the title compound as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.38 (d, *J* = 9.2, 2 H), 7.34–7.19 (m, 10 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 6.33 (d, *J* = 15.6 Hz, 1 H), 6.01 (dt, *J* = 7.2, 15.6 Hz, 1 H), 4.47 (d, *J* = 14.8 Hz, 1 H), 4.41 (d, *J* = 14.8 Hz, 1 H), 4.33–4.24 (m, 1 H), 3.81 (s, 3 H), 3.42 (t, *J* = 9.2 Hz, 1 H), 3.13 (dd, *J* = 5.6, 9.2, 1 H), 2.55–2.38 (m, 2 H); ¹³C NMR (100 MHz, CDCl₃) δ 158.3, 156.4, 136.9, 136.7, 133.7, 131.4, 128.5, 128.4, 128.0, 127.4, 127.3, 126.0, 123.9, 123.3, 114.2, 55.4, 53.6, 48.0, 46.4, 35.7; IR (film) 1698 cm⁻¹. MS (ESI): 399.2075 (399.2073 calcd for C₂₆H₂₆N₂O₂, M + H⁺).

4.3.30. (*E*)-1-Benzyl-4-cinnamyl-3-(4-methoxyphenyl)-4-methylimidazolidin-2-one (53)—Reaction of 155 mg (0.5 mmol) of 1-benzyl-3-(4-methoxyphenyl)-1-(2-methylallyl)urea with 183 mg (1.0 mmol) of β -bromostyrene for 1.5 h according to the general procedure afforded 177 mg (86%) of the title compound as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.34–7.18 (m, 12 H), 6.93 (d, J = 9.2 Hz, 2 H), 6.32 (d, J = 16 Hz, 1 H), 6.16–6.05 (m, 1 H), 4.55 (d, J = 15.2 Hz, 1 H), 4.34 (d, J = 15.2 Hz, 1 H), 3.83 (s, 3 H), 3.31 (d, J = 8.8 Hz, 1 H), 2.99 (d, J = 8.8 Hz, 1 H), 2.51 (ddd, J = 1.2, 6.8, 14.4 Hz, 1 H), 2.25 (ddd, J = 0.8, 7.6, 14.0 Hz, 1 H), 1.29 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.4, 158.5, 137.1, 136.8, 134.0, 130.8, 128.9, 128.4, 128.4, 128.0, 127.4, 127.2, 126.0, 123.9, 114.1, 59.7, 55.3, 53.2, 47.9, 42.3, 25.6; IR (film) 1698 cm^{-1} . MS (ESI): 435.2047 (435.2048 calcd for $\text{C}_{27}\text{H}_{28}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.3.31. ($\pm$)-(*E*)-(4*R*,5*R*)-1-Benzyl-3-(4-methoxyphenyl)-5-methyl-4-[3-(trimethylsilyl)allyl]imidazolidin-2-one (54)—Reaction of 155 mg (0.5 mmol) of 1-benzyl-1-(but-3-en-2-yl)-3-(4-methoxyphenyl)urea with 179 mg (1.0 mmol) of 2-bromovinyltrimethylsilane for 1 h according to the general procedure using Nixantphos in place of Xantphos afforded 187 mg (92%) of the title compound as a clear oil. This compound was isolated as a 10:1 mixture of diastereomers as judged by ^1H NMR analysis. The crude reaction mixture contained a 7:1 mixture of diastereomers. Data are for the major diastereomer. ^1H NMR (500 MHz, CDCl_3) δ 7.38–7.27 (m, 7 H), 6.90 (d, J = 9.0 Hz, 2 H), 5.77 (dt, J = 6.5, 18.5 Hz, 1 H), 5.54 (d, J = 18.5 Hz, 1 H), 4.83 (d, J = 15.5 Hz, 1 H), 4.13 (d, J = 15.0 Hz, 1 H), 3.80 (s, 3 H), 3.76–3.70 (m, 1 H), 3.33–3.25 (m, 1 H), 2.44–2.37 (m, 1 H), 2.32–2.23 (m, 1 H), 1.19 (d, J = 6.5, 3 H), -0.03 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.9, 156.4, 139.9, 137.3, 135.3, 131.6, 128.5, 128.0, 127.2, 124.2, 114.1, 61.3, 55.3, 52.4, 45.2, 38.8, 18.6, -1.5 ; IR (film) 1699 cm^{-1} . Anal calcd for $\text{C}_{24}\text{H}_{32}\text{N}_2\text{O}_2\text{Si}$: C, 70.55; H, 7.89; N, 6.86. Found: C, 70.66; H, 7.95; N, 6.81.

4.3.32. ($\pm$)-(*E*)-(1*R*,8*aR*)-1-(But-2-enyl)-2-(4-methoxyphenyl)hexahydroimidazo[1,5-*a*]pyridin-3-(5*H*)-one (55)—Reaction of 130 mg (0.5 mmol) of *N*-(4-methoxyphenyl)-2-vinylpiperidine-1-carboxamide with 121 mg (1.0 mmol) of 1-bromo-1-propene for 40 min according to the general procedure afforded 130 mg (87%) of the title compound as a brown oil. The crude reaction mixture contained a 1.5:1 mixture of diastereomers as judged by ^1H NMR analysis. Upon purification the compound was obtained as a 1.6:1 mixture of diastereomers. Data are for the mixture. ^1H NMR (400 MHz, CDCl_3) δ 7.32–7.24 (m, 2 H), 6.88 (d, J = 9.2 Hz, 2 H), 5.64–5.42 (m, 1 H), 5.36–5.24 (m, 1 H), 3.99 (d, J = 12.0 Hz, 1 H), 3.79 (s, 3 H), 3.76–3.65 (m, 1 H), 3.28–3.16 (m, 1 H), 2.74 (dt, J = 3.2, 13.2 Hz, 1 H), 2.41–2.14 (m, 2 H), 1.94–1.86 (m, 1 H), 1.82–1.74 (m, 1 H), 1.67–1.52 (m, 4 H), 1.50–1.31 (m, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.0, 156.1, 131.8, 129.0, 125.0, 123.8, 114.1, 60.7, 56.9, 55.4, 40.8, 34.5, 31.0, 24.7, 23.4, 18.0; IR (film) 1699 cm^{-1} . MS (ESI): 323.1729 (323.1735 calcd for $\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.4 Selective Deprotection of 22

4.4.1 1-Benzyl-4-(2-methylbenzyl)imidazolidin-2-one (24)—A round bottom flask was charged with 1-benzyl-3-(4-methoxyphenyl)-4-(2-methylbenzyl)imidazolidin-2-one (**22**) (77 mg, 0.2 mmol) and CH_3CN (2 mL). The resulting solution was cooled to 0 $^\circ\text{C}$, and a solution of ceric ammonium nitrate (329 mg, 0.6 mmol) in water (3 mL) was slowly added over 3 min. The reaction mixture was warmed to rt and stirred for 2 h. The reaction mixture was then transferred to a separatory funnel and extracted with EtOAc (3×5 mL). The combined organic layers were washed with saturated aqueous Na_2SO_3 (15 mL), saturated aqueous NaHCO_3 (15 mL), and brine (15 mL). The organic layer was then dried over anhydrous Na_2SO_4 , filtered, and concentrated *in vacuo*. The crude product was purified via flash chromatography on silica gel to afford 41 mg (73%) of the title compound as a yellow solid, m.p. 91–96 $^\circ\text{C}$. ^1H NMR

(400 MHz, CDCl_3) δ 7.38–7.31 (m, 2 H), 7.31–7.24 (m, 3 H), 7.17–7.09 (m, 3 H), 7.08–7.02 (m, 1 H), 4.62 (s, 1 H), 4.38 (s, 2 H), 3.92–3.80 (m, 1 H), 3.38 (t, $J = 8.4$ Hz, 1 H), 3.03 (dd, $J = 6.0, 8.8$ Hz, 1 H), 2.79 (d, $J = 7.2$ Hz, 2 H), 2.27 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.4, 137.0, 136.2, 135.2, 130.6, 129.6, 128.6, 128.0, 127.4, 126.9, 126.2, 49.9, 49.7, 47.4, 39.0, 19.5; IR (film) 3242, 1697 cm^{-1} . MS (ESI): 303.1461 (303.1473 calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}$, $\text{M} + \text{Na}^+$).

4.4.2 1-(4-methoxyphenyl)-5-(2-methylbenzyl)imidazolidin-2-one (25)—A flame-dried three-necked round bottom flask was cooled under a stream of argon and equipped with a dry ice/acetone cold finger. The flask was cooled to -78°C and charged with liquid ammonia (30 mL). Li wire (20 mg, 3 mmol) was added and the solution turned blue. The solution was stirred at -78°C for 5 min and then a solution of 1-benzyl-3-(4-methoxyphenyl)-4-(2-methylbenzyl)imidazolidin-2-one (**22**) (116 mg, 0.3 mmol) in THF (10 mL) was added. The resulting mixture was stirred at -78°C for 40 min, then a solution of diphenyl ether (320 μL , 6 mmol) in THF (20 mL) was added and the mixture immediately turned clear. The solution was warmed to rt and 1 mL of water was added. The resulting mixture was concentrated *in vacuo*, and the crude product was purified by flash chromatography on silica gel to afford 82 mg (92%) of the title compound as a white solid, m.p. $126\text{--}131^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 7.36 (d, $J = 9.2$ Hz, 2 H), 7.19–7.10 (m, 3 H), 7.10–7.04 (m, 1 H), 6.94 (d, $J = 8.8$ Hz, 2 H), 4.99 (s, 1 H), 4.50–4.37 (m, 1 H), 3.82 (s, 3 H), 3.44 (t, $J = 8.4$ Hz, 1 H), 3.27 (dd, $J = 5.6, 8.0$ Hz, 1 H), 3.09 (dd, $J = 3.6, 14.0$ Hz, 1 H), 2.70 (dd, $J = 10.4, 14.0$ Hz, 1 H), 2.24 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.9, 157.0, 136.3, 134.9, 130.9, 130.5, 129.6, 126.8, 126.0, 125.1, 114.4, 57.6, 55.4, 43.0, 35.6, 19.4; IR (film) 3247, 1704, cm^{-1} . MS (ESI): 319.1412 (319.1422 calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_2$, $\text{M} + \text{Na}^+$).

4.5 Assignment of Product Stereochemistry

4.5.1 Stereochemistry of 34–36 and 54—The stereochemistry of **34** was assigned by ^1H NMR nOe experiments as shown below.

The stereochemistry of **35–36** and **54** was assigned based on analogy to **34**.

4.5.2 Stereochemistry of 38 and 55—The stereochemistry of **38** was assigned by ^1H NMR nOe experiments as shown below.

The stereochemistry of **55** was assigned based on analogy to **38**.

4.5.3 Stereochemistry of 39—The stereochemistry of **39** was assigned by ^1H NMR nOe experiments as shown below.

4.5.4 Stereochemistry of 47–49—The stereochemistry of **47** was assigned by single crystal x-ray analysis as shown below.

The stereochemistry of **48–49** was assigned based on analogy to **47**.

4.5.5 Stereochemistry of 50—The stereochemistry of **50** was assigned by ^1H NMR nOe experiments as shown below.

4.5.6 Stereochemistry of 51—The stereochemistry of **51** was assigned by ^1H NMR nOe experiments as shown below.

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34. The increased reactivity of cyclic alkenes relative to acyclic Z-disubstituted alkenes may be due to ring strain. For additional discussion on the effect of ring strain on reactivity in Pd-catalyzed reactions involving alkene insertion, see: (a) James DE, Stille JK. J Am Chem Soc 1976;98:1810–1823. (b) Larock RC, Baker BE. Tetrahedron Lett 1988;29:905–908. (c) Ozawa F, Hayashi T, Koide H, Yamamoto A. J Chem Soc, Chem Commun 1991:1469–1470.
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Scheme 1.
Catalytic Cycle

Scheme 2.
Formation of Oxidative Cyclization Products

Scheme 3.
Formation of Isomer **51**

Scheme 4.
Stereochemistry of 4,5-Disubstituted Imidazolidine Formation

Scheme 5.
Stereochemistry in the Carboamination of **30** and **31**

Table 1

Optimization Studies.^a

Entry	Ligand	NMR Ratio 5:6	NMR Yield 5 ^b
1	dppb	1:1	24%
2	$\text{P}(o\text{-tol})_3$	5:1	22%
3	dppf	100:0	30%
4	dppe	2:1	24%
5	Dpe-phos	100:0	42%
6	Xantphos	100:0	50% (59%) ^c

^a Conditions: 1.0 equiv substrate, 1.2 equiv 4-bromotoluene, 1.2 equiv NaOtBu , 1 mol % $\text{Pd}_2(\text{dba})_3$, 2 mol % ligand (chelating ligands) or 4 mol % ligand (monodentate ligands), toluene (0.25 M), 110°C .

^b NMR yields were measured against phenanthrene as an internal standard.

^c Isolated yield is indicated in parentheses.

Table 2
Synthesis of *N,N*-Disubstituted-4-Benzyl Imidazolidin-2-one Derivatives^a

Entry	Urea	Aryl bromide	Product	Yield ^b	Entry	Urea	Aryl bromide	Product	Yield ^b
1				59	8				97
2				73	9				83
3				58	10				92
4				63	11				85
5				68	12				75
6				35	13				71
7				80	14				96

^a Conditions: 1.0 equiv substrate, 1.2 equiv ArBr, 1.2 equiv NaOtBu, 1 mol % Pd₂(dba)₃, 2 mol % Xantphos, toluene (0.25 M), 110 °C.

^b Average isolated yields obtained from two or more experiments.

Table 3

Synthesis of 4,4- and 4,5-Disubstituted Imidazolidin-2-ones^a

Entry	Urea	Aryl bromide	Product	dr ^b	Yield ^c
1				12:1 (8:1)	88
2				>20:1 (>20:1)	83
3				>20:1 (>20:1)	21
4				-	30
5				20:1 (11:1)	78
6				>20:1 (>20:1)	87
7				-	77

Entry	Urea	Aryl bromide	Product	dr ^b	Yield ^c
8			41	-	89
9	33		42	-	97

^a Conditions: 1.0 equiv substrate, 1.2 equiv ArBr, 1.2 equiv NaOtBu, 1 mol % Pd₂(dba)₃, 2 mol % Xantphos, toluene (0.25 M), 110 °C.

^b Diastereomeric ratios are for isolated products. Diastereomeric ratios in parentheses were observed in crude reaction mixtures.

^c Average isolated yields obtained from two or more experiments.

Table 4
Synthesis of Imidazolidin-2-ones Generated from Internal Alkenes^a

Entry	Urea	Aryl bromide	Product	d _r ^b	Yield ^c
1	43 4:1 E:Z		47	>20:1	50
2	44		48	>20:1	74 ^d
3			49	>20:1	65 ^d
4	45		50	>20:1	84

Entry	Urea	Aryl bromide	Product	d ^b	Yield ^c
5				>20:1	46 ^e

^a Conditions: 1.0 equiv substrate, 1.2 equiv ArBr, 1.2 equiv NaOtBu, 1 mol % Pd₂(dba)₃, 2 mol % Xantphos, toluene (0.25 M), 110 °C.

^b Diastereomeric ratios are for isolated products and were unchanged from diastereomeric ratios observed in crude reaction mixtures.

^c Average isolated yields obtained from two or more experiments.

^d Conditions: 1.0 equiv substrate, 1.2 equiv ArBr, 1.2 equiv Cs₂CO₃, 2 mol % Pd(OAc)₂, 2 mol % Xantphos, dioxane (0.25 M), 100 °C.

^e PEt₃•HBF₄ (4 mol %) was used in place of Xantphos as ligand.

Table 5

Synthesis of 4-Allyl-imidizolidin-2-ones^a

Entry	Urea	Aryl bromide	Product	dr ^b	Yield ^c
1				-	74
2				-	85
3				10:1 (7:1)	91 ^d
4				1.6:1 (1.5:1)	87

^a Conditions: 1.0 equiv substrate, 2.0 equiv ArBr, 2.0 equiv NaOtBu, 1 mol % Pd₂(dba)₃, 2 mol % Xantphos, toluene (0.25 M), 110 °C.

^b Diastereomeric ratios are for isolated products. Diastereomeric ratios in parentheses were observed in crude reaction mixtures.

^c Average isolated yields obtained from two or more experiments.

^d Nixantphos was used as a ligand in place of Xantphos.